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See Also SAUNDERS ADVERTISEMENT on Page 3

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AUGUST 23, 1941

SOME IMMEDIATE PROBLEMS FACING THE RADIOLOGIST

CHAIRMAN'S ADDRESS

RAYMOND C. BEELER, M.D.

INDIANAPOLIS

One does not have to put one's good ear to the ground to hear the rumbling sound of sudden changes and world shaking events. That these are extremely troubled times throughout the world goes without saying. It is evident that America has emphatically to assume again the role of a vigorous world power in order to remain the permanent sanctuary of certain genuinely American ideals; that, whether we like it or not, America is destined to complete the task it should have completed twenty years ago and to become, as it surely is fitted and capable of becoming, the dominant director of the nations of the world. Whether this is the actual shape of things to come for this country, time alone will tell. It hardly seems that it can be otherwise, however, as America now enters on the world scene with full mobilization of her military and her industrial resources.

What has this by-pass into the world picture to do with the subject of this paper? Primarily this: Revolutionary epochs necessitate great changes, great adjustments, great dangers and a multitude of problems. We are living in such an epoch. If we do not realize this at the outset, we can have no proper perspective of all our present day problems.

American medicine, especially in its nontechnical divisions, has gigantic problems facing it on every hand. There are economic, legal and organizational problems pertaining to national defense. American radiology as one of the very technical and complex subdivisions of American medicine shares each of the major issues facing the whole of organized medicine but, in addition to these more general problems, it has a considerable number of difficulties peculiar to its own domain. The first of these problems I wish to consider is whether or not medical radiology is to become simply a state or federal operated laboratory procedure.

The revolutionary changes in American economic and social thought over the past several years have presented American medicine with the most trying days in all its postwar history. The wide swing of the pendulum of political, legislative and even judicial thought in the United States toward socialist and collectivist doctrines has enveloped the medical profession in a legal battle the outcome of which cannot fail to have far reaching consequences for us all.

Radiology is in the most forward echelon of this conflict, placed there by the complex nature of its equipment and technics and its absolute indispensability to all institutions furnishing complete medical care. It is determined not to become merely a federal or state controlled laboratory procedure. That this problem has perilously endangered our branch of the healing art arises from certain conditions and situations that have made our group especially vulnerable. We have been in the vanguard in every struggle tending to force wider and wider development of hospital insurance plans to include special medical service. The roentgenologist, the pathologist and the anesthetist have borne the brunt of the battle to date against the strenuous attempts of group hospitalization insurance plans to include radiology and other medical service in their insurance coverage.

The momentum gained by group hospitalization insurance programs, movements known as medical service plans, sickness insurance and so on, together with the gigantic inroads made by the federal government in the field of cancer diagnosis and treatment, has placed us in the greatest jeopardy. Unquestionably, the radiologist and his specialty are being used as an opening wedge through which other branches of medical practice are to be pushed for the future hospital domination over the practice of medicine. It makes little difference whether the hospital administrator, executive or superintendent is operating for a large metropolitan group hospitalization plan or is a member of the ever increasing federal bureaucracy now preparing to extend its functions into actual diagnosis and treatment of cancer; the prime objective seems to be to override any admittedly rational arguments of professional unsoundness in their plans by pouring on the public a constant din of half truths concerning the economically profitable nature of the proposed plans.

Are we going to be able to convince the public that more formidable progress against cancer can be achieved by private radiologists than under bureaucratic federal clinics? Can we convince the public that private radiologists are better qualified to prescribe the correct roentgenographic or therapeutic procedure than the most prominent hospital insurance executive? It would would seem that no such task of convincing the public ought to be necessary, but a vast portion of the opposition is politically inspired, politically subsidized and politically controlled. The problem seems gigantic and overwhelming. It can be solved and our mission can be accomplished only if we close ranks, if the individual radiologist will forsake selfish considerations and join with the majority opinion of his colleagues for the duration of our emergency, prove to the public that we are not in any disagreement among ourselves and inform and educate as rapidly as possible any of our confrères who may still be unaware of what is going on and where these radical trends are taking us.

Remarkable advancement has been made lately in the field of radiology as it relates to technics developed for

Read before the Section on Radiology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

rapid and economic roentgen studies of the chest, suitable for extensive surveys of large groups of persons. The great need and desirability of an accurate and economical technic for such work is recognized by every one and is not limited to the tuberculosis worker or the public health specialist. But here again a major problem is presented to us with both an economic and a technical aspect. The prime difficulty arises from the fact that because such a method for wide scale roentgenographic chest studies has been brought to the present state of development the forces who will gain most from its correct and accurate use cannot wait longer for further perfection of the technic. They clamor for wholesale chest studies while the technic they wish admits of a degree of error far greater than these zealous guardians of the public health would tolerate in any other procedure. Yet, because radiologists wish to proceed more cautiously and hence more scientifically, they are put in the disagreeable position of appearing to hold up the development and widespread application of fluorography and miniature roentgenograms (so-called 4 by 5 films). No one will claim that this method is completely perfected today. The checking of errors by conventional roentgenography is still required. The necessary preliminary accumulation of statistical data and thorough studies into the limits of the method were not allowed to be brought to a conclusion before a wholesale demand for the general use of miniature roentgenograms was made by certain groups—largely the hyphenated lay-medical agencies engaged in tuberculosis work, military induction boards and certain public health divisions.

An urgent plea is made for careful, painstaking development of this work with due regard to all its aspects, scientific accuracy, economic fairness to the individual patient in the survey group and to the radiologist performing the work and interpreting the roentgenogram and, above all, a holding off of hurried and ill considered utilization of the method simply because partially informed groups with loud voices want a mass method used on all the masses before that method is thoroughly perfected.

Another important problem which radiologists have to consider is the fact that certain manufacturers of roentgen ray equipment are willing and anxious to sell equipment to unqualified practitioners of medicine. The fact that many general practitioners have been led to believe that the installation and operation of a roentgen ray unit and the proper interpretation of films made with it is as simple a matter as ordering, installing and using an electric sterilizer is due for the most part to the avid commercialism of numerous smaller, unethical supply houses and roentgen ray manufacturers. Their number has increased greatly of late and their clientele includes as well the chiropractor, the naturopath and the electrotherapeutist. The outstanding feature of their work is their unique job of salesmanship. They have convinced certain physicians that, first, such a complex piece of electrical engineering requires only the knowledge needed to snap a button on and off and, second, that with the film made so easily its correct interpretation is a matter of even less effort. How they can convince their buyer that roentgen therapy requires no more than mail order knowledge I have never been able to understand.

That this is an ever growing menace is self evident to all of us assembled here. That this is a very real danger, let me cite a case with which I am familiar: Mr. A, a representative of an ethical and reliable roentgen ray manufacturing firm, was recently called to the office of physician X, whose apparatus had suddenly ceased to function. On going over the apparatus, Mr. A discovered that the machine showed unmistakable signs of having either been operated at extremely high milliamperage or having been used for extremely long exposures. Dr. X emphatically stated that during the three months he had possessed the machine he had used it no more than four or five times and then for but five to ten seconds for fluoroscopic work only. Closer inspection of the equipment showed that, while these examinations were being made by Dr. X, the machine had been operating at 15 to 20 milliamperes, and still closer scrutiny showed not even a piece of plate glass for protection in the fluoroscopic screen. Simply the fluorescent screen and no glass whatever. Mr. A began inquiring of Dr. X whether he had noted any changes about the skin of his face or hands. The doctor stated "Now that you mention it, I had noticed my eyes would have the most peculiar burning sensation in them a few hours after each fluoroscopic examination." Was it not a fortunate thing that the physician's apparatus failed to operate one day before he had suffered further injury?

Caveat emptor is the legal phrase in commercial law demanding that the buyer beware. For physicians foolish enough to feel that combined general practice and radiology is the field for them, there is no phrase, legal or otherwise, with which to warn them.

Aside from the possibility of the inherent physical dangers to both the general practitioner and his patient, many physicians seem totally unaware of the gigantic technical strides made in radiology since Roentgen's remarkable discovery. Radiology is no longer of such compact size or simplicity as to be considered an adjunct or sideline to any other branch of medicine. This seems too commonplace a statement to require mention, but it is amazing how many general practitioners and even certain specialists have failed to realize the many intricate subdivisions already required within the field of radiology. It is readily understood that organized radiology requires a prolonged training period for those anxious to be qualified members in it. Also that any one not taking the required course and time in preparation for the proper understanding of this science is little more than an impostor.

Last but not least of these questions before roentgenologists today is the rapid increase in size, cost and complexity of the apparatus required to perform thorough work in our field. It puts a complicated financial problem to the recently qualified young radiologist anxious to enter on the practice of his chosen specialty. The huge initial cost of equipment, high rental fee for the large office or floor space required for it, cost of expandable supplies needed, such as films and chemicals for processing them, darkroom apparatus and filing and record equipment all in addition to the salary expense of necessary clerical and technical assistants make the young radiologist's problems greater than those of any other beginning specialist. Many hospitals have taken advantage of this financial dilemma of the young radiologist to maneuver him into a position of semidependence. To be sure, not all hospitals are to be so indicated, but it has been one of the paramount means whereby certain of them have been enabled to preach the heresy of radiologic service being part and parcel of hospitalization and so through their group hospitalization insurance plans place our specialist in

the predicament discussed as problem one at the beginning of this paper.

The opportunities afforded competent radiologists to enter practice are still great. As long as medical practice in the hospitals remains medical practice and does not become hospital practice, many institutions can supply opportunities for certified radiologists. In fact, many hospital radiologic departments could double or triple the number of certified men on their present staffs with much benefit both to patients and to the visiting staff. Additional opportunities are to be found for the young radiologists throughout the smaller communities in numerous small county hospitals. No competent young radiologist need feel that this apparent financial obstacle is insurmountable, for the competent man can make his way as always.

In closing, I wish to remind you that only a few of the problems facing the members of our section have been discussed. Those of the greatest importance are being discussed by authoritative contributors to the various radiologic publications, men who are endeavoring to maintain our security now and to marshal all our available strength for the battles that lie ahead.

The important task for us all is to exert our utmost efforts, individually and collectively, to make the majority opinion of our specialty and of all organized medicine prevail, so that medical practice will continue to be run by medicine and radiologic practice by radiologists despite the tremendous upheavals occurring in the world about us.

23 East Ohio Street.

TREATMENT OF SEPTIC THROMBOPHLEBITIS OF THE CAVERNOUS SINUS

CHAIRMAN'S ADDRESS

LEROY A. SCHALL, M.D.

BOSTON

One of the most fatal complications occurring in otolaryngology is that of septic thrombophlebitis of the cavernous sinus. Previous to the advent of chemotherapy Eagleton [1] was able to report but 3 recoveries by surgical methods out of 25 cases. Browder and Myerson [2] had a recovery after introducing a sterile clot proximal to the infection. Grove [3] surveyed the literature and came to the conclusion that septic thrombophlebitis of the cavernous sinus was practically 100 per cent fatal. Since the introduction of chemotherapy isolated case reports of recovery are beginning to appear in the literature. Barnshaw,[4] Seydell [5] and Pace [6] each report a recovery following the use of sulfanilamide and Morrison and Schindler [7] one after the use of sulfapyridine.

Read before the Section on Laryngology, Otology and Rhinology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. Eagleton, Wells P.: Cavernous Sinus Thrombophlebitis, New York, Macmillan Company, 1926.
2. Browder, Jefferson, and Myerson, M. C.: A Surgical Method for the Prevention of Thrombophlebitis of the Cavernous Sinus, Arch. Otolaryng. **21**: 574 (May) 1935.
3. Grove, W. E.: Septic and Aseptic Types of Thrombosis of the Cavernous Sinus, Arch. Otolaryng. **24**: 29-50 (July) 1936.
4. Barnshaw, H. P.: Report of a Case of Bilateral Cavernous Sinus Thrombosis: Recovery Without Operative Intervention, J. M. Soc. New Jersey **36**: 22 (Jan.) 1939.
5. Seydell, E. M.: Recovery from Thrombosis of the Cavernous Sinus, Arch. Otolaryng. **30**: 429 (Sept.) 1931.
6. Pace, Errett: Thrombosis of the Cavernous Sinus, Arch. Otolaryng. **33**: 216 (Feb.) 1941.
7. Morrison, Lewis F., and Schindler, Meyer: Cavernous Sinus Thrombosis: Report of Recovery Following Sulfapyridine Therapy, Arch. Otolaryng. **31**: 948 (June) 1940.

That there are two types of thrombosis of the cavernous sinus, the one septic and the other sterile, has been accepted clinically and proved at autopsy.[8] My discussion will be limited to the septic type exclusively. The anatomy of the cavernous sinus has been

Fig. 1 (case 1).—Patient's appearance at the time of admission.

described by many authors [9] and will not be reviewed again. The routes of extension of septic processes to the cavernous sinus have been well described by Eagleton.

To establish the diagnosis of septic thrombophlebitis of the cavernous sinus, Eagleton [1] proposed the following diagnostic criteria:

1. A known site of infection.
2. A blood stream infection.
3. Early signs of venous obstruction.
4. Involvement of the nerves in the sinus.
5. Neighborhood abscess of the soft parts.
6. Symptoms of complicating disease.

It has been my privilege to observe 3 cases of septic thrombophlebitis of the cavernous sinus presenting a symptomatology that fulfilled the criteria as established by Eagleton. In these 3 cases recovery occurred following the use of chemotherapeutic agents combined with heparin. That heparin is an important adjunct in treatment is demonstrated by case 2, in which the cavernous involvement developed while the patient was under treatment with chemotherapeutic agents for a nasal furunculosis.

The use of heparin in conjunction with chemotherapeutic agents was suggested to me by Dr. Champ Lyons of the Massachusetts General Hospital, and the treatment was carried out under his direction. The first 2 cases have been reported by Lyons.[10] To the best of our knowledge, these cases of septic thrombophlebitis of the cavernous sinus were the first in which therapy with these agents was given.

In discussing the use of heparin, Bancroft [11] speculates: "For the septic processes occurring in association with otolaryngology, it would seem advisable to combine chemotherapy with heparin. The combination

8. Lewis, E. R.: Cavernous Sinus Thrombosis with Recovery Proved by Necropsy, Ann. Oto-Rhino-Laryng. **43**: 1084-1090 (Dec.) 1934.
9. Eagleton.[1] Browder and Myerson.[2] Grove.[3] Morrison and Schindler.[7]
10. Lyons, Champ: The Treatment of Staphylococcal Cavernous Sinus Thrombophlebitis with Heparin and Chemotherapy, Ann. Surg. **113**: 113 (Jan.) 1941.
11. Bancroft, Frederic W.: Use of Anticoagulants in Cases of Postoperative Thrombosis and Embolism, Arch. Otolaryng. **32**: 934 (Nov.) 1940.

of the sulfanilamide group and heparin should aid in prevention of spread of septic emboli and in stabilization of the clot when it is impossible to ligate the vein proximally."

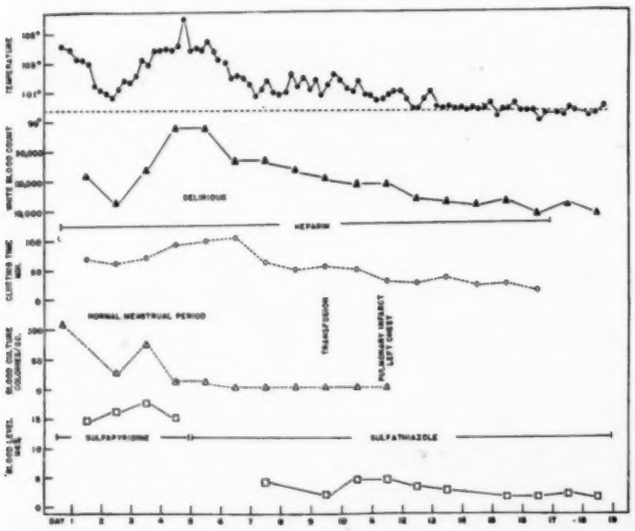

Fig. 2.—Course of temperature, white blood cell count, clotting time, blood culture (colonies per cubic centimeter) and treatment in case 1.

Heparin is a strong organic acid, probably a mucoitin trisulfuric acid, discovered and described by Howell.[12] It was first isolated from liver, and investigations gave support to the view that it is a normal constituent of

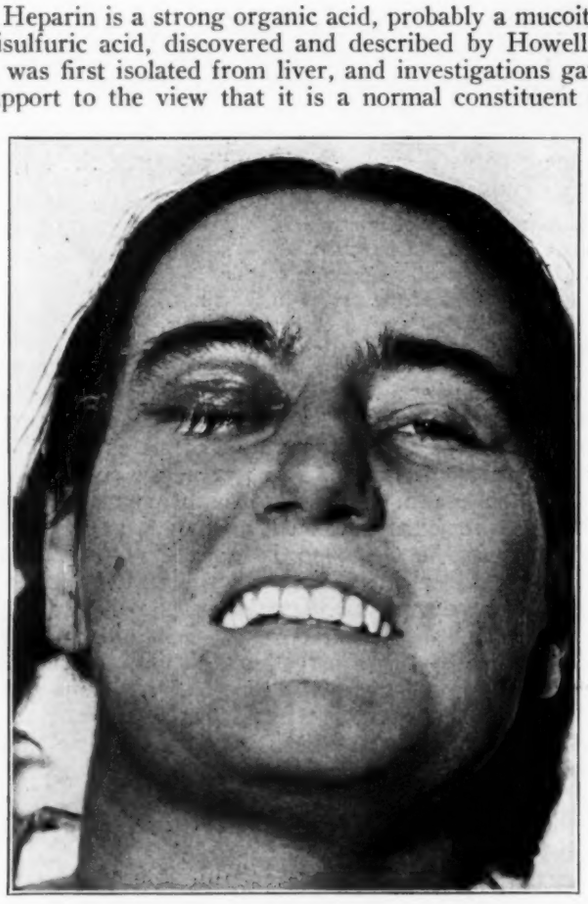

Fig. 3 (case 1).—Patient's appearance nine weeks after admission.

the blood plasma. Improved methods of extraction and purification by Howell,[13] by Charles and Scott[14] and by Schmitz and Fischer[15] have rendered heparin safe to use in man.

Early experiments showed that heparin has a distinctive effect in preventing the coagulation of the blood. Howell advanced the theory that it is the inhibiting factor responsible for the fluidity of the blood, that it is not an antithrombin but that it prevents coagulation by a reaction with prothrombin, which interferes with the activation of prothrombin to thrombin. Murray[16] reached the deduction that heparin also has an important effect on blood platelets in that it prevents their clumping and thereby prevents thrombosis.

Heparin has now been used in many conditions in which thrombosis is a factor—surgery of blood vessels,[17] venous grafts,[18] embolectomy,[19] periphlebitis,[11] malignant endocarditis[20] and sudden vascular occlusion.[11]

Fig. 4 (case 2).—Patient's appearance at the time of admission.

Heparin is administered by a constant intravenous saline drip. Usually 1,000 units of heparin, i. e., 10 mg., is added to each 100 cc. of saline solution. The saline and heparin solution is permitted to run into the patient's vein at such a rate that the clotting time of the patient's blood is maintained at the desired level.[10] In these cases the clotting time of the blood was maintained at about ninety minutes as determined by the five tube method.

12. Howell, W. H.: Two New Factors in Blood Coagulation—Heparin and Proantithrombin, Am. J. Physiol. **47:** 328 (Dec.) 1918.
13. Howell, W. H.: The Purification of Heparin and Its Presence in Blood, Am. J. Physiol. **71:** 553 (Feb.) 1935.
14. Charles, A. F., and Scott, D. A.: Studies on Heparin: IV. Observations on the Chemistry of Heparin, Biochem. J. **30:** 1927-1933 (Oct.) 1936.
15. Schmitz, Adolf, and Fischer, Albert: Ueber die chemische Natur des Heparins: 11. Die Reindarstelling des Heparins, Ztschr. f. physiol. Chem. **216:** 264-273 (May 3) 1933.
16. Murray, D. W. G.; Jaques, L. B.,; Perrett, T. S., and Best, C. H.: Heparin and Thrombosis of Veins Following Injury, Surgery **2:** 163 (Aug.) 1937.
17. Murray, D. W. G.: Heparin in Surgical Treatment of Blood Vessels, Arch. Surg. **40:** 307 (Feb.) 1940. Murray, Jaques, Perrett and Best.[10] Bancroft.[11] Murray and Best.[18]
18. Murray, D. W. G., and Best, C. H.: Heparin and Thrombosis: The Present Situation, J. A. M. A. **110:** 118 (Jan. 8) 1938. Bancroft.[11] Murray.[17]
19. Murray.[17] Murray and Best.[18]
20. Kelson, Saul R., and White, Paul D.: A New Method of Treatment of Subacute Bacterial Endocarditis, J. A. M. A. **113:** 1700 (Dec. 4) 1939.

REPORT OF CASES

CASE 1.—A woman aged 31, seen in consultation with Dr. Vincent J. Kelley on April 5, 1940, had a nasal furuncle of five days' duration and had received small doses of sulfanilamide at home for three days.

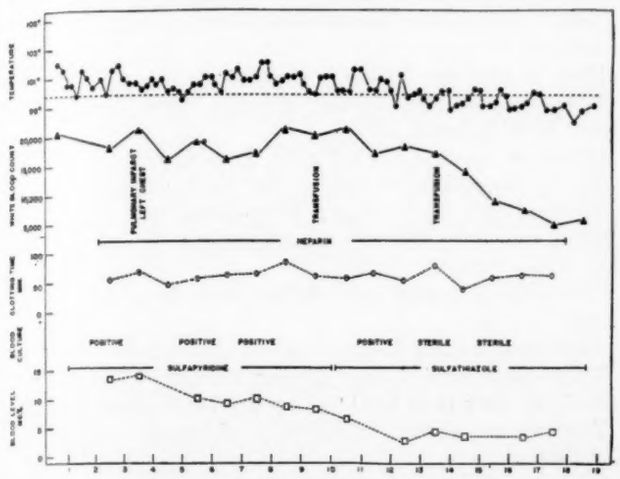

Fig. 5.—Course of temperature, white blood cell count, clotting time, blood culture (colonies per cubic centimeter) and treatment in case 2.

With the development of the signs and symptoms of cavernous involvement, Dr. Kelley was called and the patient was admitted to the Massachusetts Eye and Ear Infirmary.

On examination the patient was irrational, the temperature was 104.3 F. and there were exophthalmos of the right eye

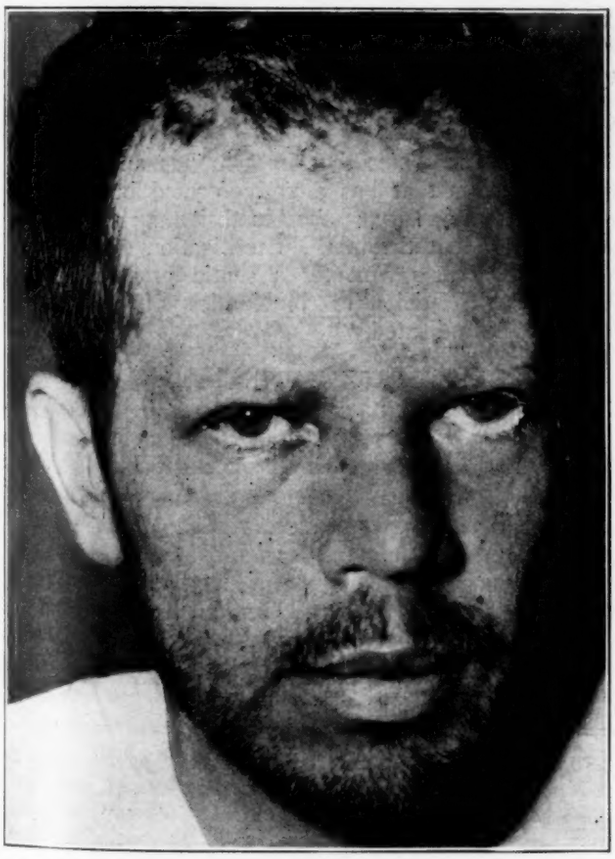

Fig. 6 (case 2).—Patient's appearance four weeks after admission.

and edema of the bridge of the nose and both right eyelids. There was a discharging furuncle of the right naris, and the frontal veins were palpable.

In consultation, Dr. Lyons suggested the use of heparin in conjunction with chemotherapy, and the treatment was carried out under his direction. The treatment and course of the disease may be rapidly reviewed by the following clinical notes:

First hospital day: Heparin and sulfapyridine started.

Fourth hospital day: Sulfathiazole substituted for sulfapyridine, as the blood culture showed staphylococci.

Eleventh hospital day: Pulmonary infarct.

Seventeenth hospital day: Heparin stopped after a total dose of 225,000 units.

Twentieth hospital day: Sulfathiazole stopped.

Thirty-fourth hospital day: Clinical signs of meningitis confirmed by lumbar puncture. Sulfapyridine started.

Forty-ninth hospital day: Meningitis still present. Sulfathiazole substituted for sulfapyridine.

Fifty-seventh hospital day: Afebrile and symptomatically improved.

Seventy-seventh hospital day: Discharged home; taking sulfathiazole.

At the time of discharge there was a partial paralysis of the third nerve and complete paralysis of the fourth nerve on the

Fig. 7 (case 3).—Patient's appearance at the time of admission.

right. Chemotherapy was continued for a total period of four months, at the end of which time the spinal fluid protein had returned to normal.

On May 15, 1941 the patient was admitted to the psychiatric ward of the Massachusetts General Hospital suffering from a paranoid-like attack, the exact nature of which has not as yet been determined.

CASE 2.—A man aged 41, an engineer, entered the Massachusetts Eye and Ear Infirmary May 14, 1940 with the diagnosis of acute frontal sinusitis of one week's duration. Physical examination revealed a nasal furunculosis, and the diagnosis of acute sinusitis was not supported. On entry he was started on sulfapyridine therapy, but by the fourth hospital day exophthalmos of the right eye and edema of the eyelids and the bridge of the nose developed, with palpable frontal veins. Heparin was started on the fourth day and stopped on the nineteenth after a total dose of 580,000 units. During the course of the disease involvement of the sixth and the first division of the fifth cranial nerve developed. Sulfathiazole was substituted for sulfapyridine on the eleventh hospital day because blood cultures showed staphylococci.

Sulfathiazole was given for three months, at the end of which time the spinal fluid protein was normal. The patient still has a residual hyperesthesia of the left frontal region.

CASE 3.—A boy aged 9 years, referred to me on Jan. 7, 1941 by Dr. Charles W. Geddes with a diagnosis of cavernous sinus

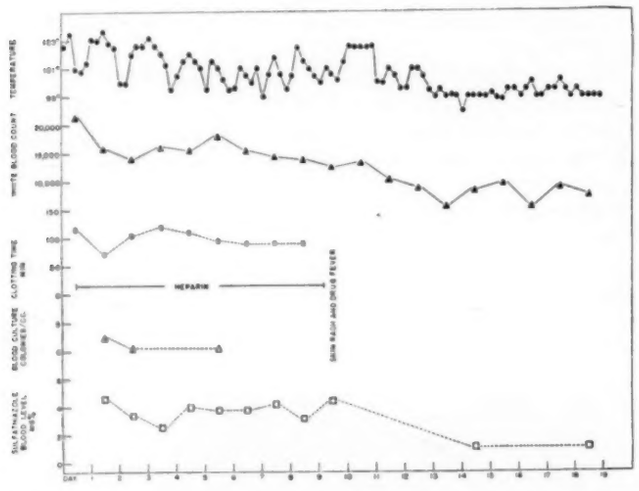

Fig. 8.—Course of temperature, white blood cell count, clotting time, blood cultures (colonies per cubic centimeter) and treatment in case 3.

thrombosis, was awakened from sleep three days before entry by a pain in his nose with some swelling of the face. His father noticed a small elevated area inside the left nostril. Under flaxseed poultices the swelling became worse and a furuncle in the nose broke and discharged.

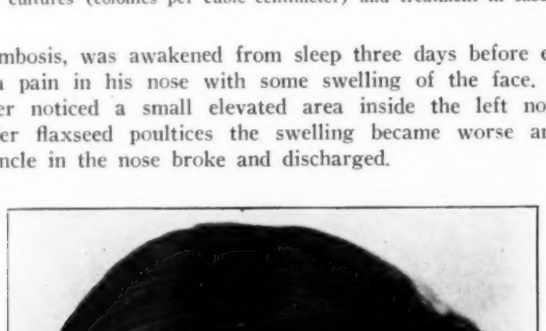

Fig. 9 (case 3).—Patient's appearance four weeks after admission.

On admission to the hospital there were exophthalmos and edema of the right eyelid and the bridge of the nose. The temperature was 102 F., and there was headache, with stiffness of the neck and a slight Babinski reflex on the right side. The patient was drowsy, and blood cultures were positive for staphylococci. The patient was placed under the care of Dr. Lyons, and the hospital record can be summarized as follows:

First hospital day: Heparin 20,000 units given with sulfathiazole. Slight bleeding from nose.

Second hospital day: Sixth nerve paralysis.

Third hospital day: Involvement of first and second division of fifth nerve.

Ninth hospital day: Heparin stopped.

Tenth hospital day: Lumbar puncture done. Fluid crystal clear. Initial pressure 125.

Eighteenth hospital day: Patient up in chair.

Twenty-fourth hospital day: Sulfathiazole stopped.

Twenty-eighth hospital day: Temperature rose to 100.8 F. Pain on coughing; lumbar puncture, no increase in pressure—clear fluid, 1 cell.

Twenty-ninth hospital day: Sulfathiazole started again; temperature 102 F.

Thirty-fourth hospital day: Patient symptom free.

Thirty-ninth hospital day: Patient discharged home—sulfathiazole ½ grain (0.03 Gm.) twice a day for six to eight weeks.

Total amount given: 130,000 units of heparin and 108 Gm. of sulfathiazole.

COMMENT

Three consecutive cases that fulfilled the diagnostic criteria of Eagleton of septic thrombophlebitis of the cavernous sinus of the anterior type have ended in recovery after treatment by the combination of chemotherapy and heparin.

Lyons[10] states: "There is reason to believe that staphylococcal bacteremia usually arises from foci of septic thrombophlebitis in and around areas of suppuration. Such a conception indicates that the attack upon any staphylococcal bacteremia should attempt to prevent the extension of septic thrombi as well as to destroy the bacteria."

It is contended not that heparin has any influence on a thrombus that has already formed but that, by increasing the fluidity of the blood, it may prevent the extension of that thrombus. Sterilization of the blood and the thrombus converts a septic process into an aseptic one, so that the combination of these drugs seems to be indicated.

CONCLUSIONS

1. Three consecutive patients with bacteremic staphylococcic thrombophlebitis of the cavernous sinus of the anterior type have been successfully treated by a combination of chemotherapy and heparin.

2. Sulfathiazole, given in doses sufficient to maintain a blood level of 5 mg. per hundred cubic centimeters and continued for a long period after administration of the heparin has been discontinued, has been the chemotherapeutic agent of choice. Experience with sulfadiazine indicates that this may prove to be the present drug of choice.

Fuel Values.—Nutrition laboratories have, as the result of many experiments, determined the average loss of fuel value in the body from these sources and, after deducting for such losses, give the following figures as the "physiological" fuel value of the three foodstuffs: 1 gram of pure carbohydrate, 4 calories; 1 gram of pure fat, 9 calories; 1 gram of pure protein, 4 calories. It is important to remember that the fuel value of fat is 2¼ times that of carbohydrate or protein, and hence foods rich in fat are especially high in fuel value.—Bogert, L. Jean, and Porter, Mame T.: Dietetics Simplified, New York, Macmillan Company, 1940.

CAISSON DISEASE

A STUDY BASED ON THREE HUNDRED CASES OBSERVED AT THE QUEENS-MIDTOWN TUNNEL PROJECT, 1938

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Caisson disease is an industrial hazard encountered in the building of bridges, tunnels and skyscrapers where compressed air is employed. In the past this malady has caused permanent disability and death in many instances. Certain principles of prophylaxis and new concepts of treatment are here presented aiming to reduce this industrial hazard.

THE CAUSATION OF CAISSON DISEASE

Caisson disease is caused by nitrogen gas, a physical agent. Emboli are produced by the formation of nitrogen gas bubbles in the tissues and blood stream which interfere with normal life processes.

A homogeneous mixture of gases in the atmosphere covers the earth to a height of approximately 4½ miles. The atmospheric pressure is the weight of these gases on the earth's surface and is expressed in pounds per square inch. Although atmospheric pressure varies slightly, it is approximately 15 pounds per square inch.

The interchange of gases in the lungs and blood of a person who is in a compressed air atmosphere obeys the law of physics governing the solution of a gas in a liquid.[1] The quantity of nitrogen and oxygen dissolved by the blood varies directly as the pressure. The increased amount of oxygen absorbed is readily metabolized because it is an active gas chemically. This is not true of nitrogen, which is inert and is not utilized by the body.[2]

The increased amount of nitrogen dissolved in the blood is absorbed by the various tissues of the body according to their ability to hold nitrogen in solution. Fat and fatty tissues will dissolve much more nitrogen because nitrogen is five times more soluble in fat than in other tissues and body fluids.[3] The amount of tissue saturation with nitrogen depends on the amount of air pressure and the length of time the body is exposed to this pressure.

When a person who has worked in compressed air is exposed immediately to normal atmospheric pressure, a phenomenon occurs similar to the sudden opening of a bottle of charged water. For example, bubbles of carbon dioxide will evolve from the charged water and will continue until equilibrium of partial pressures of carbon dioxide in the atmosphere and in the liquid is obtained. A similar phenomenon occurs in the blood and the body tissues under sudden release of pressure. The dissolved nitrogen gas evolves in the form of bubbles, producing blocking of the circulation and tearing of tissues with resultant symptoms of caisson disease. Bert's experiments add further evidence for the support of the nitrogen gas emboli theory as the cause of this disease.[4]

1. Travers, M. W.: The Experimental Study of Gases, New York, Macmillan Company, 1901, chapter 9.

2. The quantity of a gas dissolved by a liquid increases directly as the pressure (Henry, 1803). The quantity of a gas dissolved by a liquid from a mixture of gases depends on the partial pressure of that particular gas (Dalton, 1807).[1]

3. Hill, Leonard: Caisson Sickness and the Physiology of Work in Compressed Air, London, E. Arnold, 1912; An Address on Compressed Air Illness and Experimental Research, Brit. M. J. **1**: 348-353, 1912.

4. Bert, Paul: Communication sur les effets de l'air comprimé, Bull. Soc. méd. de l'Yonne (1872) **13** (pt. 2): 48-55, 1873.

PATHOLOGY

Accumulation of evidence from postmortem examinations further supported the gas emboli theory as the cause of caisson disease.[5] Fatal cases grouped themselves into a rapidly fatal group and a delayed fatal group. In the rapidly fatal group, death is caused by nitrogen emboli to the vital centers of the brain, the coronary vessels and the pulmonary arteries.

In the delayed death groups, death is caused by secondary complications following neurologic manifestations of the disease. After long standing paralysis of the lower extremities, bedsores, sepsis, anemia, pneumonia and exhaustion usually develop. The significant pathologic changes in the delayed death group are found in the spinal cord. The lumbar and thoracic regions of the cord show areas of necrosis and softening with degeneration and destruction of ascending and descending fibers.

SIGNS AND SYMPTOMS

Onset of Symptoms.—The onset of symptoms of the disease is relatively rapid. Of the 300 cases observed 60 per cent occurred during the first hour, 35 per cent during the second hour and 3 per cent during the third hour. Six cases occurred after twelve hours, amounting to 2 per cent of the total.

Presenting Symptoms.—Pain (the "bends"): The presenting symptom of the disease was pain. The cases observed formed groups clinically as follows: pain generalized, pain localized and pain with prostration and collapse. The pain of compressed air disease may vary in intensity, depending on the site of bubble formation and the amount of gas evolved in the tissues. The pain may thus be mild and transient or severe and excruciating. The occurrence of pain in various parts of the body according to incidence is as follows: legs 50 cases, unilateral or bilateral, occurring generally about the knees and ankles; arms 60 cases, unilateral and bilateral, involving several joints. It may radiate or follow the course of a peripheral nerve. Abdominal bends may be of such severity that shock, collapse and prostration occur, forming the next clinical group. Here pain in the abdomen is outstanding. It is often accompanied by signs of circulatory collapse because of the great amount of gas in the abdominal vessels mechanically impeding the circulation. The appearance of mottling and blotching with subcutaneous hemorrhages is further evidence denoting large amounts of free gas in the circulation. These are prodromal signs of coma and collapse, which should be carefully watched for. To the compressed air worker these symptoms are known as the "bends." The reason for this vernacular expression is obvious. The pain is of such severity as to make the afflicted one bend over to obtain relief. The pain is caused by the presence of bubbles of nitrogen gas in the tissues and the plugging of small arteries by nitrogen gas emboli. The lodging of nitrogen gas emboli in the gastrointestinal and mesenteric vessels is undoubtedly the cause of abdominal bends. Likewise, when bubbles of gas form in unyielding structures and tissues of the body such as ligaments, fascia, connective tissue, periosteum, synovial membranes, muscle spindles, joint capsules, skin and sweat glands, pain is the result. The greater the amount of gas, the greater will be the stretching of the unyielding tissues with the resultant increase in pain. Most compressed air workers suffer on decompression

5. Bert, Paul: La pression barométrique; recherches de physiologie expérimentale, Paris, G. Masson, 1878.

with mild fleeting pains in the various parts of the body which should be differentiated from true caisson disease.

Vertigo (the "staggers"): Next in the order of incidence are the cases in which symptoms resembling Ménière's syndrome are outstanding. The symptoms are dizziness or vertigo, staggering or loss of equilibrium, nausea or vomiting, abnormal ocular movements (nystagmus) and tinnitus, or ringing in the ears. Of the 30 cases observed at the Queens-Midtown Tunnel in 1938, there was vertigo in 6, vomiting and vertigo in 6, vertigo, vomiting, staggering and nystagmus in 10 and vertigo, nausea and tinnitus in 8. These symptoms are evidently caused by the evolution of nitrogen bubbles in the internal ear, labyrinth, cochlea and semicircular canals. To the compressed air worker this syndrome is known as the "staggers." A worker suffering from the "staggers" resembles a man who has indulged in alcoholic excess. Unless the worker's identifying badge is seen, the man is believed to be an alcoholic addict and is treated as such. This is one important reason why compressed air workers should wear their identifying badge where it can be readily seen and detected.

Air Hunger (the "chokes"): Dyspnea is characteristic of this group. These patients appear acutely ill and present a condition which is alarming. However, they yield readily to treatment, provided it is given immediately. Compressed air workers suffering from this symptom complex resemble an asthmatic patient. Physical examination of the chest reveals bilateral medium and fine moist and musical rales. These patients also resemble persons with heart disease suffering with sudden left ventricular failure and transitory pulmonary edema. This clinical picture is familiar to the compressed air worker and is known as the "chokes." Fifteen cases of the "chokes" were observed at the Queens-Midtown Tunnel. The symptoms are caused by varying amounts of nitrogen emboli in the pulmonary arteries.

Cutaneous Manifestations (the "itch"): The various cutaneous manifestations noted in the cases studied were pruritus (the "itch"), erythema and mottling and blotching. There were 20 cases presenting cutaneous manifestation of the disease: 6 presented only pruritus, 5 a combination of pruritus, erythema and blotching of the skin. Erythema and mottling of the skin were present in 6 cases. The intense itching is caused by nitrogen bubbles in the sweat glands of the skin. The erythema and purplish mottling of the skin denote stasis of blood in the cutaneous vessels as a result of nitrogen emboli in the skin capillaries. Cutaneous signs are usually early signs of compressed air illness. They signify possible ensuing symptoms of much greater severity. Therefore persons presenting cutaneous manifestations should be carefully observed for severer symptoms. Of 6 cases in which mottling and blotching of the skin were present, the "staggers" developed in 2 and the "chokes" in 4.

Neurologic Manifestations: This group of cases is important from the point of view of its disabling character and the possibility of permanent damage to the central nervous system. Patients with central nervous system symptoms who are not treated promptly are apt to develop permanent disability.

The nerve cells and tissues of the central nervous system are vulnerable to ischemia and pressure from nitrogen bubbles with consequent pressure necrosis. Thus the reasons for permanent damage can readily be seen. Nitrogen bubble formation can occur in any part of the brain or spinal cord. Nitrogen emboli can form locally in the blood vessels or be carried to the central nervous system by the blood stream from other parts of the body. The central nervous system symptoms produced by compressed air disease can simulate those caused by any other disease or injury of the central nervous system. Complete unconsciousness and collapse to numbness and tingling of an extremity can be expected.[6]

Paralysis of the bladder and bowels is common in spinal cord cases. The majority of afflicted persons recover with treatment, while some remain with permanent weakness of the lower limbs. In some instances the patient dies after a lingering illness, death being caused by secondary complications such as cystitis, pyelonephritis, bedsores, pneumonia, exhaustion and anemia. Twenty-five cases of central nervous system symptoms occurred at the Queens-Midtown Tunnel: with brain involvement, hemiplegia 3 cases, monoplegia 2 cases, internal strabismus 2 cases, nystagmus 2 cases, diplopia 2 cases; with spinal cord involvement, sensory, numbness and tingling of both legs 5 cases, motor, paresis of both legs 4 cases, paralysis of both legs 2 cases, sensory and motor disturbance, numbness and tingling and paresis 3 cases. Urinary and bowel incontinence are present in all spinal cord cases in addition to the symptoms mentioned. Recovery was complete with treatment except in 1 case of paralysis of both legs. Urinary and bowel control were regained but weakness of both limbs remained.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of caisson disease is not difficult. Although the symptoms are varied and depend on the parts of the body involved, there should be no doubt as to the diagnosis provided the patient is conscious and can give a history of exposure to compressed air during the preceding twelve hours. The identification badge that the compressed air worker wears conclusively confirms the diagnosis. It is conceivable that the identifying badge might not be worn and the worker might be in coma and unable to give a history. Furthermore, compressed air workers are susceptible to other injury or illness in addition to caisson disease. In such instances the diagnosis becomes more difficult and a careful differential is always necessary. A severe case of abdominal bends can simulate an acute surgical condition of the abdomen and conversely an acute surgical condition of the abdomen can simulate abdominal bends. True caisson disease must be differentiated from mild cases of myalgia, arthralgia and neuralgia. Aside from caisson disease, 135 cases of mild pain in the extremities were observed. Most of these cases responded to physical therapy and medication. The pains were located chiefly in the joints and extremities. They were described as vague aches and pains in the thighs, legs, arms, knees, ankles, elbows, wrists, shoulders and along the course of the peripheral nerves. The pains

6. Clark, E. A.: Effects of Increased Atmospheric Pressure upon the Human Body, M. Arch., St. Louis **5**: 1-30 and 295-300, 1870-1871. Cazamian: Hématomyélie par décompression brusque chez un scaphandrier; paraplégie spasmodique, Arch. de méd. nav. **98**: 212-224, 1912. Genet, L.: Atrophie optique partielle et maladie des caissons, Bull. Soc. d'opht. de Paris, 1933, pp. 318-321. Callan, L. W.: Double Choked Disks Associated with Compressed Air Disease (Caisson Disease), Arch. Ophth. **36**: 509-512, 1907. Boinet: La maladie des scaphandriers, Bull. Acad. de méd., Paris **55**: 756-764, 1906. Bassoe, Peter: Compressed Air Disease, J. Nerv. & Ment. Dis. **38**: 368-369, 1911; The Late Manifestations of Compressed Air Disease, Tr. XV Internat. Cong. Hyg. & Demog. (1912) **3**: 626-638, 1913.

were transitory and not severe enough to incapacitate the patient but were aggravated with change in temperature.

Physical examination revealed three clinical groups as follows: pains limited to muscles, myalgias; pains limited to joints, arthralgias; pains limited to the course of a peripheral nerve, neuralgias. Combinations of the three groups were also seen. It is believed that these cases are the result of the decided change in temperature on compression and decompression, the unusually damp atmosphere of the tunnel environment and the poor local tissue circulation resulting from fatigue following strenuous physical effort.

COMPLICATIONS

The complications of caisson disease are limited to the bones and joints. The symptoms of onset are insidious and are delayed from six months to a year or more following repeated attacks of the disease. A case of bone necrosis was reported in 1888 by Twynam.[7] Cases of chronic arthritis were reported by Bornstein and Plate[8] in 1911 and 1912 following repeated attacks of the disease. Bassoe[9] in 1913 reported several cases of arthritis deformans. Christ[10] in 1934 reported joint lesions. It is possible that nitrogen emboli in end arteries of nutrient vessels to bones might cause necrosis and degenerative changes in bone. Four cases of aseptic bone necrosis attributed to caisson disease were reported by Kahlstrom, Burton and Phemister[11] in 1939.

PROGNOSIS

The mortality of caisson disease has dropped to an exceedingly low figure at the present time because of the efficiency of the recompression treatment. Prior to the use of the medical lock the mortality rate was high. Blick[12] in 1909 reported 30 per cent mortality among pearl divers, 60 out of 200 patients dying before medical aid could be given. Jaminet[13] in the St. Louis bridge construction reported 119 cases with permanent paralysis in 52 and death in 14, representing a 14 per cent mortality. Domínguez[14] reported 106 cases of serious paralysis with 14.9 per cent mortality. During the building of the Brooklyn bridges the mortality was 3 per cent. During the work on the Hudson River tunnels the advantages of recompression were amply shown on the installation of a medical lock. After the medical lock was employed the mortality rate dropped from 25 per cent to 1 per cent. The mortality rate in building the Pennsylvania Railroad East River tunnels was 2 per cent. In 300 cases observed during the building of the Queens-Midtown Tunnel there was no mortality from this disease. In cases of sudden collapse and unconsciousness the prognosis is graver than in cases presenting only pain in the extremities. Those in which paralysis is present are difficult to cure, and advice as to the outcome should be guarded.

7. Twynam, G. E.: A Case of Caisson Disease, Brit. M. J. **1**: 190, 1888.

8. Bornstein and Plate: Ueber chronische Gelenkveränderungen entstanden durch Presslufterkrankung, Fortschr. a. d. Geb. d. Röntgenstrahlen **18**: 197-206, 1911-1912.

9. Bassoe, Peter: Compressed Air Illness, Illinois M. J. **17**: 462-469, 1910.

10. Christ, A.: Ueber Caissonkrankheit mit besonderer Berücksichtigung einer typischer Erkrankung des Hüftgelenkes, München. med. Wchnschr. **81**: 843, 1934.

11. Kahlstrom, S. C.; Burton, C. C., and Phemister, D. B.: Aseptic Necrosis of Bone, Surg., Gynec. & Obst. **68**: 129-146 (Feb.) 1939.

12. Blick, G.: Notes on Diver's Paralysis, Brit. M. J. **2**: 1796-1798, 1909.

13. Jaminet, A.: Physical Effects of Compressed Air, St. Louis, R. & T. A. Ennis, 1878.

14. Dominguez, A. G.: Caisson Disease o parálisis de los buzos, Rev. de med. y cir. de la Habana. **17**: 359-368, 1912.

PROPHYLAXIS AND PREVENTION

In addition to nitrogen embolus formation, certain secondary conditions predispose an individual toward caisson disease. They are age, systemic disease, obesity, alcoholism and fatigue.

It is the consensus that the ideal age for compressed air workers is between 20 and 40 years, since during these years the cardiovascular system is at its peak of greatest efficiency and best able to withstand the hardship of increased air pressure. Diseases of the heart, lungs and kidneys and peripheral vascular diseases are grounds for rejection. These conditions should be carefully ruled out during the first examination. Obese men are bad risks because of the great solubility of nitrogen in fat. Men who are known to be habitual drinkers are poor risks because of the effect of alcohol on the circulation and should be rejected.

A man who is acutely ill should not be admitted to compressed air until he has recuperated. Acute infection of the upper respiratory passages should temporarily disqualify a man for employment, because the infection usually involves the eustachian tubes and ostiums of the sinuses, causing adhesions of the walls and consequent closure. When one is entering the compression chamber the ear drum is stretched, causing severe pain. This is known as "ear block." Infection of the mucous membrane of the ostiums of the sinuses causes acute edema. Valvelike action occurs, allowing air to enter the sinus; but its escape is prevented. Air under pressure becomes trapped in the sinus, causing severe pain. This is known as "sinus block." Acute infection of the sinus may follow from organisms driven into the sinus by the compressed air, requiring surgical intervention. Failure of the eustachian tubes to open to equalize the pressure on either side of the tympanic membrane will result in rupture of the tympanum with consequent infection of the middle ear.[15] Fatigue predisposes to emboli and the "bends" because of its effect on the circulation, causing slowing of the elimination of nitrogen gas.

There is no immunity to caisson disease. Consequently the most important step in the prophylaxis is the physical examination with special emphasis on the heart, lungs, circulatory system, circulatory efficiency and cardiac reserve. The importance of age, weight and habits should not be overlooked.

Approximately 20 per cent of the men examined at the East River tunnels were rejected. Men who show symptoms of caisson disease after one or two trial test shifts would be rejected. Many of the men suffer from repeated mild attacks of pain and itching of the skin, but there is no need for rejection on such mild symptoms.

The ultimate prevention of the disease depends on the proper elimination of nitrogen from the tissues during decompression. There is only one route by which the nitrogen in the body tissues and blood can be eliminated, and that is through the lungs by the circulation. Any condition affecting the efficiency of the circulation is likely to affect the efficiency of the elimination of the nitrogen gas from the tissues. During the decompression stage the value of exercise in stimulating the circulation cannot be overemphasized. The extreme importance of slow decompression should always be borne in mind. The working time under

15. Crosson, J. W.; Jones, R. R., and Sayers, R. R.: Helium-Oxygen Mixtures for Alleviation of Tubal and Sinus Block in Compressed Air Workers, Pub. Health Rep. **55**: 1487-1496, 1940. Lovelace, W. R., II; Mayo, C. W., and Boothy, W. M.: Aero-Otitis Media, Proc. Staff Meet. Mayo Clin. **14**: 9-96, 1939.

pressure should always be held within safe limits with adequate rest periods between shifts. This is important, because the amount of nitrogen absorbed depends to a large extent on this time factor. The inhalation of oxygen and oxygen-helium mixtures during the decompression period to hasten the nitrogen release from the body is a valuable prophylactic measure. Sudden changes in temperature should be avoided. Therefore the temperature of all air locks should be controlled by suitable heating apparatus to keep the temperature as constant as possible.

TREATMENT

The essential treatment of caisson disease is the return of the patient to the compressed air. In previous years, men who were seized with an attack voluntarily returned to the compression chamber for the relief of their symptoms. Today this treatment is given in a compression chamber known as a "medical air lock." [16]

Only those who have witnessed the treatment of a case of compressed air illness can realize the efficacy of recompression. Recompression should be started as soon after the onset of symptoms as possible, because the sooner the bubbles of nitrogen are redissolved the sooner will the circulation be established and pain relieved. The possibility of permanent damage to vital structures such as the brain and spinal cord will be materially reduced by immediate recompression. It has been noted that if treatment is delayed following the onset of symptoms a higher pressure is necessary to give relief. Long delay in recompression may result in permanent injury to the cord because of anemia as a result of the circulation being blocked by nitrogen emboli. It is true that recovery will occur in certain mild cases without recompression, but there are no criteria by which we can determine which cases suddenly become serious. It is most advisable therefore to treat all definitely diagnosed cases of the disease by recompression immediately.

Of 300 patients treated at the Queens-Midtown Tunnel airlock, 85 per cent were completely relieved, 12 per cent were partially relieved and 3 per cent had no relief. Experience has established that symptoms in most cases are relieved by recompression to a pressure equal to that to which the worker was exposed. Occasionally it is necessary to go 5, 10 or 15 pounds higher before complete relief is obtained.[17]

The consensus favors waiting twenty to thirty minutes before starting the decompression process. Observations have proved that this waiting period has given the best result. In many instances symptoms recurred if decompression was started immediately with no waiting period, requiring another recompression. To avoid repeated recompressions, it was found advisable to introduce this waiting period before starting the decompression process. Despite the waiting period, however, symptoms are apt to recur requiring one or more additional recompressions.

It was noted that if the men were made to exercise the affected limb during the decompression process it aided materially in obtaining a permanent relief. The inhalation of pure oxygen and oxygen-helium mixtures during decompression has given encouraging results in many instances. These gases hasten the elimination of dissolved nitrogen from the blood and hence decrease the tendency toward the disease.[18] The importance of stimulating drugs as adjuncts in treatment should not be minimized. Strychnine, epinephrine and caffeine are valuable circulatory stimulants and one should not hesitate to use these drugs in cases of circulatory collapse. In cases of respiratory failure, artificial methods should be instituted. Physical therapy and general nursing care should be given whenever necessary.

16. The first recompression chamber in the United States was installed during the building of the New York Hudson tunnels under the North River in 1894. This was known as a "medical lock" and because of its efficiency it was made essential to the equipment of all compressed air work.

17. Keays, F. L.: Compressed Air Illness with a Report of 3,690 Cases, Pub. Cornell Univ. M. Coll., Dept. Med. **2**: 1-55, 1909. Shilling, C. W.: Compressed Air Illness, U. S. Nav. M. Bull. **36**: 9 and 235, 1938.

SUMMARY

1. Three hundred cases of caisson disease occurred without mortality during the building of the New York-Queens Midtown Tunnel in 1938.

2. Serious disability in these cases was also practically nil. This remarkable result may be attributed to:

The selection of workers between the ages of 20 and 40 years, free from acute or chronic disease and with freedom from pulmonary, cardiovascular, renal, peripheral vascular or gastrointestinal diseases and obesity.

Prompt recompression of all subjects exhibiting the slightest symptoms of caisson disease, thereby minimizing neurologic phases of the disease, which ordinarily when neglected prove most disabling or fatal.

The prophylactic inhalation of oxygen and oxygen-helium mixtures in the decompression stage, thus hastening nitrogen release.

The rigid regulation of the duration of the working shifts and rest period between shifts according to prescribed pressure-time codes.

20 West Seventy-Second Street.

RADIATION PROTECTION IN FORTY-FIVE HOSPITALS

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AND
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The increasing use of radiation in medicine, industry and research demands increased knowledge of radiation effects and protection methods. The authors visited forty-five hospitals of all types, ranging in size from forty-four to over three thousand beds (thirty-two have more than two hundred beds) and studied storage and handling of radium, calibration and shielding of roentgen therapy equipment and technics of use and shielding of roentgenographic and fluoroscopic units.

Ionization chambers ranging in sensitivity from 0.25 roentgen to 100 roentgens full scale were used in making measurements. Estimates of average exposures were calculated from ionization measurements made during typical operations such as preparation of radium applicators and roentgenoscopic and roentgenographic procedures, multiplied by the average daily time spent performing such activities. Adequacy of equipment and practices were judged in most instances on the basis of recommendations for protection which have been pub-

18. Behnke, A. R., and Yarbrough, O. D.: Physiologic Studies of Helium: Report on Use of Helium Oxygen Mixtures for Diving, April 1939. Behnke, A. R., and Shaw, L. A.: The Use of Oxygen in the Treatment of Compressed Air Illness, U. S. Nav. M. Bull. **35**: 61-73, 1937.

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lished by various writers[1] and those in the National Bureau of Standards handbooks on roentgen ray[2] and radium protection.[3] The authors used the 0.1 roentgen dose which is published in these handbooks as the safe daily tolerance dose.

RADIUM

Relationships between amounts of radium, distance from the nearest person to the radium and time spent at such distance were studied, and it was found that lead equivalents of storage blocks were such that overexposure occurred in sixteen of the forty-five hospitals and was borderline in thirteen. Storage in safes in administration offices was a frequent cause of excessive exposure of nontechnical personnel. Radium units, especially those in assembled applicators, were found outside the storage blocks in more than one fourth of the hospitals.

Fourteen institutions had no L blocks, and ten had blocks less than 2 inches (5 cm.) in thickness. Four of these were less than ¼ inch (0.64 cm.) thick. Radium was often assembled in more than one place in the hospital, yet only one L block and set of assembly instruments had been provided.

Instruments for assembly were excellent in twenty-four institutions. In the remainder, either no special instruments had been provided or those at hand were inadequate. Frequent use of fingers was noted during manipulation. Lack of education and supervision of subordinate personnel often contributed to overexposure. Table 1 shows the exposures found during the assembly of single applicators for intra-uterine use.

Hands, paper boxes, glass jars and inadequate lead boxes were used as carriers in the majority of the institutions.

ROENTGEN DIAGNOSIS

Roentgen departments had excellent lead-lined control rooms in twenty-three of the forty-five hospitals. Thirteen had no protection for the operator except that around the tube, and this usually was incomplete or insufficient. The remainder had only partial lead protection.

Many technicians held the majority of infants and patients speaking only a foreign language who came for roentgenograms, and one received exposures on the hands as high as 35 roentgens while holding a single patient. Other daily exposures ranging from 1 to 5 roentgens were observed.

Open lead glass bowls were found to be in frequent use. The majority of technicians working with them did not have the benefit of adequate shielding at the control panel and received daily doses in excess of 0.1 roentgen. Four instances were noted in which the unshielded operator at the control panel was in the direct beam of the tube, and one of these received 0.2 roentgen a day doing only sinus series.

In several instances the holding of films or patients during portable roentgenography resulted in overexposure. In one case the hands received 0.42 roentgen and the body 0.14 roentgen during the making of two exposures.

The greatest repeated overexposures were found during fluoroscopy. The worker depends on inherent protection in the equipment and other protective devices such as lead-rubber aprons and gloves to shield him from overexposure, because it is impossible to do fluoroscopy at a distance in a shielded control room.

The lead glass in the fluoroscopic screen provided adequate shielding in all institutions; however, it was found that the shutters of thirty of the units did not restrict the direct beam to the protected screen area. There was considerable overlapping when the shutters were wide open with the screen 40 cm. above the table top. Since average intensities at the surface of the table were approximately 13 roentgens a minute without a patient at 75 kilovolts and 5 milliamperes, it was possible for the examiner to receive large doses on his hands if he worked with the shutter wide open and no protective gloves. A careful check revealed that most radiologists were unaware of the fact that often they opened widely one or the other pair of leaves of the shutter at intervals during each examination, especially during examinations of chests and bones. Hand-held portable screens were found to be great offenders in permitting overexposure.

TABLE 1.—*Body and Finger Exposures in Selected Cases During Assembly of a Single Radium Tandem for Intra-Uterine Insertion*

Case	Applicator Material	Radium: In Applicator, Mg.	Radium: Other on Table, Mg.	L Block Thickness, In.	Forceps Length, In.	Elapsed Time, Min.	Exposure in Roentgens: Body	Exposure in Roentgens: Fingers
A	Rubber	85	275*	2	10	31	0.02	25.0
B	Silver	90	10	¾	8	12	0.04	0.4
C	Rubber	75	None	None	10	10	0.06	1.8
D	Rubber	75	125*	None	4	20	0.08	36.0

* In open lead box.

Average exposures to the hands of the examiner during fluoroscopy were found to be such that doses could not be held under 0.1 roentgen a day unless gloves with 0.5 mm. of lead equivalent were worn as a routine. In spite of this, one fourth of the radiologic departments possessed no lead rubber gloves, or such gloves were never used. The practice of wearing pigskin or canvas gloves, offering inadequate protection during typical fluoroscopic examinations, was found to be frequent. In the institutions in which gloves were used, many of the gloves were found to be old and to have missing lead protection on the sides of the fingers or other local defects, thus failing to provide efficient protection.

Fluoroscopic rooms were checked at various points for stray radiation with a hand screen, and it was found that there was sufficient scattering in twenty-seven such rooms to permit resolution of the bones of the fingers 10 feet from the table with the units operating at 75 kilovolts and 5 milliamperes. Aprons were checked for effectiveness in reducing the exposure hazard in these hospitals, and extreme variations were found in the protective value of the aprons owing to sizable differences in their lead content. Aprons with 0.5 mm. lead equivalents placed on the table top in the direct beam reduce the intensity at the screen to such a level that no fluorescence can be seen on it. Many aprons were found to have lead equivalents well under 0.5 mm., and in one case eight thicknesses of apron in the direct beam permitted sufficient fluorescence to occur to enable one to examine bones of the hand. Aprons were worn by technicians in the fluoroscopic examination rooms of

1. Taylor, L. S.: X-Ray Protection, J. A. M. A. **116:** 136-140 (Jan. 11) 1941. Pack, G. T., and Livingston, E. M.: Treatment of Cancer and Allied Diseases, New York, Paul B. Hoeber, Inc., 1940, vol. 1, pp. 274-300. Failla, Gioacchino: Radium Protection, Radiology **19:** 12-21 (July) 1932. Kaye, G. W. C.; Bell, G. E., and Binks, W.: The Protection of Radium Workers from Gamma Radiation, Brit. J. Radiol. **8:** 6-26 (Jan.) 1935. Quimby, Edith: Radium Protection, J. Appl. Physics **10:** 598-608, 1939.

2. X-Ray Protection: Safety Recommendations, Prepared by Advisory Committee on X-Ray and Radium Protection, Handbook HB20, United States Department of Commerce Bureau of Standards, 1936.

3. Radium Protection: Handbook HB23, United States Department of Commerce, Bureau of Standards, 1938.

only seven hospitals, although scattering was of such intensity in many of the rooms as to permit them to receive more than 0.1 roentgen a day. It is noteworthy that the age of the equipment was not found to be a factor in the levels of overexposure discovered.

ROENTGEN THERAPY

Thirty-nine of the forty-five hospitals visited had equipment for high voltage roentgen therapy. Only four in this group had inadequate shielding, although the technic used in a few of the others caused occasional overexposure. Shifting of patients with the tube in operation and failure to close the lead protective door were the principal faulty technics noted.

Calibrations were checked in thirty-seven of the institutions. Table 2 shows the errors found with reference to frequency of calibration. One fourth of the calibrations in use had errors of more than 10 per cent. Most of the errors were such that fewer roentgens were delivered in a given period of time than the calibration in use indicated. Of the twenty hospitals calibrating oftener than once a year, only three had

TABLE 2.—*Distribution of Calibration Differences Over 10 per Cent with Reference to Frequency of Calibration*

Calibration Frequency	Hospitals	Hospitals with Differences Greater Than 10 per Cent	Calibration Differences, per Cent
2 or more per month	1	0	0
1 per month	9	3	10, 12, 15
2 per year	10	0	0
1 per year	11	4	15, 19, 46, 50
1 per 2 years or more	6	2	15, 19

TABLE 3.—*Calibration Differences of More Than 10 per Cent by Profession of Worker Calibrating*

Profession of Calibrator	Institutions in Which Calibrators Worked, Number	Errors Over 10 per Cent, Number
Registered physicists	11	0
Radiologists and staff physicists *	16	1
Technicians	3	2
Others	7	6

* Includes residents in radiology.

differences, and none of these exceeded 15 per cent. Six of the remaining seventeen institutions in which calibrations were checked once a year or less often showed errors, the greatest of which was 50 per cent.

Table 3 shows the errors with reference to the person calibrating. In the twenty-seven hospitals in which registered physicists, radiologists or staff physicists made the measurements, only one of the calibrations in use was found to be in error. Eight of the ten institutions in which technicians and others calibrated had errors of more than 10 per cent.

The principal reasons for the differences found were as follows: (1) Calibrations were too infrequent, (2) persons calibrating were not thoroughly familiar with the proper methods of doing such work, (3) local calibration equipment was not standardized and (4) stop watches, timers and integrating devices gave erroneous readings. The first two were the principal causes of variations.

INJURY

Extensive study of injuries of workers was not feasible in this survey owing to time limitations; however, a few observations were made.

Blood counts were routine procedures in only nine institutions. Several instances in which total leukocyte counts fell below 5,000 and total red counts and hemoglobin content were reduced were noted, but the methods of performing counts in most cases were not objective enough to permit any real significance to be attached to them.

Cutaneous effects varying from atrophy to the formation of epithelioma were noted in twelve radiologists (20 per cent of the radiologists seen) and five technicians. The total population observed was approximately two hundred and twenty-five, of whom the majority were technicians whose employment had been relatively brief. Those with injuries had had exposures to radiation varying from ten months to twenty-five years, and the majority had been exposed more than fourteen years.

No observations on genetic injuries could be made from data available during this survey.

SUMMARY

A study of protection in forty-five hospitals has shown that there are so many points in mechanics and practices which must be carefully controlled if overexposure is to be prevented that no hospital was able to eliminate all possibility of excessive exposure. In general, hospitals tended to have good protection in most particulars or inadequate protection in most particulars.

It was found that careful compliance with the recommendations in the handbooks on radium and roentgen ray protection enabled even the busiest workers to receive daily doses in the order of 0.02 roentgen or less. However, equipment and practices, as they were found, caused a large number of the workers to receive more exposure than the recommended 0.1 roentgen a day.

In the hospitals visited, too little attention was paid to adequate education and supervision of technical workers handling radium and x-ray equipment. Many workers, other than radiologists, who used x-ray equipment and radium had little knowledge of radiation physics.

The need for adequate lead protection in storage and L blocks for radium and careful choice of site for such storage and assembly were often ignored.

Obsolete equipment and failure to provide or use lead protective barriers during roentgenography permitted many cases of overexposure to occur. Excessive exposure was found to result from the commonly observed practice of holding patients during roentgenography.

Both radiologists and technicians received considerably more radiation during fluoroscopy than they were aware of. These exposures were the most excessive noted in the survey.

It was found that less inherent protection had been built into most equipment and protective devices than radiologists generally realized. Few persons had made adequate measurements to reveal the adequacy of protection in their departments.

In one fourth of the thirty-seven hospitals in which calibrations were checked, errors exceeded 10 per cent. Radiologists and physicists were found to be the most competent groups to do calibrations. Calibrations were too frequent in many hospitals to permit accuracy in the calculation of doses given to patients.

The impression was gained by us that too little attention has been paid to protection with reference to both equipment and practices in most of the hospitals visited. The casual finding of twelve injuries among sixty

radiologists is evidence of the need for further study of tolerance doses, the problems of shielding of equipment, and operating technics.

ABSTRACT OF DISCUSSION

EDITH QUIMBY, M.A., New York: Many like to think that radiologists are so conscious of the hazards of their profession that they all make sure of adequate protection. This paper should open our eyes. All the failures reported by Drs. Scheele and Cowie have been in departments under the supervision of qualified radiologists. Some of the most flagrant examples of carelessness were made by technicians whose chiefs disclaimed knowledge of what had been occurring. This is a serious indictment—but how many of you know all of your technicians' short cuts? Do you know whether your radiographic tube can ever point at an open door? Do you know how many times your technicians are endangered by holding patients whose cooperation they cannot secure? How many of you have made sure that your lead rubber gloves and aprons have been tested, and how many of you wear them when they have been tested? How many of you know the equivalent of protection in your fluoroscopes? And how many of you know how much scattered radiation they are getting, even though you yourself may be safe? How many of you know what procedure your radium technicians go through in making up applicators, whether they fumble around with the forceps and then pick up the tubes with their fingers and jam them into place? How many of you know how long the radium applicators lie around in occupied rooms before or after they are used? There should be no need for reviewing the protection requirements; they have been published in the radiologic journals and in the bulletins of the Bureau of Standards. But it is not always easy to see just how a particular installation or procedure fits into standard recommendations. For this reason your radiologic organizations, through their standardization committees, maintain a list of registered radiologic physicists. These men and women have all passed a comprehensive examination covering calibration and protection methods, and they are available for consultation on these matters. They will go over existing installations, make complete surveys and give you their recommendations or they will go over plans and offer advice before a new installation is made. In the first case they may pick up difficulties before you get into trouble. In the second they can insure satisfactory protection, and at the same time they may be able to save you money by knowing where maximum shielding is necessary and where something less is entirely satisfactory.

DR. JOHN T. MURPHY, Toledo, Ohio: May I ask Dr. Scheele if the newly designed fluoroscopic unit for the Army has been checked for the effect of radiation on the operator? It looks to me to be the most flagrant violation of the rules of fluoroscopy that I have ever seen.

DR. LEONARD A. SCHEELE, Bethesda, Md.: In answer to Dr. Murphy's question, I do not know whether or not this equipment has been tested for scattering. While we spend a great deal of time talking about protection, many people do little to test exposure actually. Some manufacturers, for example, seem to have made few or no tests of scattering from their equipment under actual or simulated working conditions. They put a little lead here and there and assume that they have provided adequate protection. They often arrange shutters which, when they leave the factory, limit the direct beam to the screen but after a few months no longer limit it on all sides.

DR. MURPHY: Isn't it a fact that, since they have been putting the Bucky diaphragm under the fluoroscopic table, it is impossible to bring a cone into place to shield the lateral and indirect radiation from the fluoroscope?

DR. SCHEELE: It was found that that was the source of much of the secondary radiation and overexposure during roentgenoscopy. We hope that a mechanical means such as a sliding extension on the cone can be devised so that when the Bucky diaphragm is slid into place the extension will be lowered automatically and springs will push it up into place to fill the gap when the plate holder is moved aside.

FALSE POSITIVE SEROLOGIC REACTIONS FOR SYPHILIS

DUE TO SMALLPOX VACCINATIONS (VACCINIA)

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In the past few years there has been a renewal of interest in false positive serologic reactions. Partly because of the increased number of tests performed as a routine on apparently nonsyphilitic persons, there is a better realization of the number of causes of false positive reactions. There are three main groups of such reactions: (1) those due to technical error, a relatively infrequent occurrence; (2) those reactions encountered in persistently false positive human serums resulting from the presence of a reagin-like component which has been demonstrated in various animal serums;[1] (3) those positive serologic reactions which are found in patients with organic disease other than syphilis; they occur regularly in yaws, fairly constantly in leprosy and malaria and less frequently in many other diseases.[2] Further information and conclusive identification of those diseases causing positive reactions are particularly of clinical interest when the reactions are strongly positive and thus capable of leading to incorrect diagnosis.

With most diseases in which false positive reactions have been frequently reported there is little evidence as to their relative incidence or duration. In some cases the reactions remain positive for only a limited period, as in malaria and infectious mononucleosis. Early reports on serologic studies in these two diseases indicated that only 10 to 20 per cent of the patients gave positive reactions; later studies with frequently repeated tests show that a positive reaction may be expected in almost every malarial patient and in a high proportion of patients with infectious mononucleosis if the specimen is collected at the proper time.

Many acute infectious diseases are known to cause false positive serologic reactions, but vaccinia has not been generally recognized as a cause of such reactions until Moore and his co-workers recently mentioned this possibility, stating that it has been encountered in their clinic.[3] There should be particular concern as to the effect of vaccination because it is an immunologic procedure of such general application. Certainly the medical profession should have a peculiar responsibility to see that no patient is wrongly regarded as syphilitic when the false positive serologic reaction may be the result of vaccination.

In 1940 Barnard[4] reported a case in which positive reactions were observed for more than a month in the

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From the Division of Dermatology and the Students' Health Service, University of Minnesota, and the Minnesota Department of Health, Division of Preventable Diseases.

1. Giordano, A. S., and Carlson, B.: Occurrence of a Nonspecific Substance in Guinea Pig Serum Fixed by Antigen in the Wassermann Test, Am. J. Clin. Path. **9**: 130, 1939. Kahn.[9]

2. Biologic False Positive Serologic Tests for Syphilis, editorial, Ann. Int. Med. **15**: 171, 1940. Moore.[3] Thomas and Garrity.[7]

3. Moore, J. E.; Eagle, H., and Mohr, C. F.: Biologic False Positive Serologic Tests for Syphilis: III. A Suggested Method of Approach to Their Clinical Study, J. A. M. A. **115**: 1602, 1940.

4. Barnard, R. D.: False Positive Blood Serological Tests for Syphilis Following Vaccination for Variola, Illinois M. J. **77**: 78 (Jan.) 1940.

blood of a recently vaccinated person (table 1). There is some doubt that vaccinia caused the positive reactions in this case because the "primary take" did not appear until nearly three weeks after vaccination, but the evidence submitted is reasonably conclusive that vaccinia was the causative factor.

Later in 1940, Bay and Sankstone [5] decided that the facilities at the Chicago State Hospital made it an "easy matter to make a statistical examination" of this problem. They studied 100 persons on whose blood Kahn tests were performed on specimens collected at intervals from twenty-nine to seventy-six days from the onset of the vaccination take, and "in no instance was a positive reaction obtained." They concluded that the incidence of such positive reactions must be less than 1 per cent.

TABLE 1.—*False Positive Reactions in Vaccinia (Barnard), Inoculated March 11, 1938 (Delayed Vaccinia)*

	4/9	4/15	5/12	5/18	6/1
Kahn	3+	4+	4+	4+	—
Cholesterol antigen	—	...	4+	2+	—
Lipoid antigen	—	..	—	—	—

Thomas and Garrity [6] also investigated this problem with a review of the records of 10,000 naval recruits from whom the blood specimens were collected an average of twelve days after vaccination. They found that twenty-three of the twenty-six false positive Kahn reactions were encountered in the group having primary or accelerated vaccination reactions (52 per cent of the total), rather than in the group having immune reactions (48 per cent). There was no appreciable difference between the group showing primary reactions as compared with those showing accelerated reactions. Since no preliminary control studies were performed and only one type of test was used, it was impossible to estimate the percentage incidence of reactions due to vaccinia. In a second report on another group of 10,000 recruits whose blood specimens were collected only before vaccination, six (0.06 per cent) false positive Kahn reactions were recorded as compared with twenty-six (0.26 per cent) in the group vaccinated before the collection of the blood.[7] Thomas and Garrity describe 1 person whose blood previous to vaccination showed a negative and who gave strong Kahn, Kline and Wassermann reactions three weeks after vaccination. In this case the Kahn verification test was of the syphilitic type. Reactions became negative within four weeks.

TABLE 2.—*Studies on Blood of Student with Severe Primary Vaccinia*

		1/27	2/10	2/17	5/24
Laboratory A	Kolmer	3+	+	—	—
	Kline	4+	3+	±	—
Laboratory B	Kolmer	...	Positive	—	—
	Kahn	...	Positive	Positive	—

Barnard also mentioned in his report that Giordano has discussed a similar case. Though Giordano's case has not been formally recorded, he states that in 1935 he observed a patient whose blood reacted positively to a complement fixation and a precipitation test during the period of the local lesion of vaccinia. In 1941 he observed another person who had a false positive reaction associated with vaccinia. In each case the strongly positive reaction gradually changed to negative within forty-five days.[8]

Several years ago the following incident stimulated our interest in this subject. Dr. Mattie J. Bullard of Gary, Ind., then on the staff of the University of Minnesota Students' Health Service, received a report of Kolmer 3 + and Kline 4 + on blood taken from a student who had severe primary vaccinia. The results of subsequent studies are shown in table 2.

Because of the conflicting evidence as to the role of vaccinia in causing false positive reactions, the following study of serologic reactions of a group of youths not previously vaccinated was undertaken. In an effort to exclude the possibility of syphilis or a false positive reaction of undetermined origin, the blood was first tested at the time of inoculation. The subjects were requested to return for a test two weeks later, but in many cases the interval was longer. Those whose serums then gave positive or doubtful reactions were asked to submit to periodic testing until the report might become negative. In addition to those who showed a doubtful or positive reaction to the diagnostic tests, the studies were repeated on all who showed any reaction to the Kline exclusion test. The time interval of two weeks after inoculation was chosen because it was thought that the patients of Bay and Sankstone may have been studied so long after vaccination that any false positive reactions might already have returned to negative.

TABLE 3.—*Serologic Reactions in 7,601 Examinations*

	Entrance Examination	Periodic Examination	Incidence of Syphilis	False Positive or Doubtful
Men	2,692	1,875	12	35
Women	1,732	1,302	1	26
Total	4,424	3,177	13 (0.17%)	61 (0.8%)

All specimens were tested by the Kolmer Wassermann, Kline diagnostic, Hinton and Mazzini tests. Most of the specimens taken after vaccination were tested also by the Eagle and the standard Kahn test.

In any serologic study the reliability of the laboratory performing the tests must be given first consideration. In this study the facilities of the Minnesota Department of Health were used. Serologic tests as performed in these laboratories have been evaluated in the U. S. Public Health Service survey and have been compared with other laboratories within the state. Recently, in a group of patients with early syphilis, the results of standard Kahn tests in these laboratories have been compared with results reported by Dr. Kahn's laboratory on duplicate specimens. The sensitivity and specificity of the tests as performed are shown to be satisfactory.

The physical status of the persons tested also deserves consideration. They were students entering the university who submitted to a routine physical examination and demonstrated no evidence of syphilis. The incidence

5. Bay, A. P., and Sankstone, M. I.: Effects of Vaccination on Wassermann Tests, Correspondence, J. A. M. A. **115**: 475, 1940.

6. Thomas, G. E., and Garrity, R. W.: Routine Kahn Blood Reactions: Report on 10,000 Tests Made on Naval Recruits, U. S. Naval Med. Bull. **39**: 72 (Jan.) 1941.

7. Thomas, G. E., and Garrity, R. W.: Routine Kahn Blood Reactions: Supplementary Report on 20,000 Tests Made on Naval Recruits, With Observations on the Relationship of Cowpox Vaccination to the False Positive, U. S. Naval Med. Bull. **39**: 272 (April) 1941.

8. Giordano, A. S.: Personal communication to the authors.

of syphilis and of apparently false doubtful or positive reactions has been determined among students entering the university in previous years. Table 3 indicates the status of the group tested in 1939, one year before the present study.

RESULTS OF SURVEY

Among 267 persons in whom primary vaccinia later developed, all specimens taken at the time of inoculation were reported negative to the Kolmer Wassermann, Hinton and Mazzini tests. One gave a positive reaction (2 +) and 3 gave doubtful reactions to the Kline diagnostic test. These 4 reactors are not included in this report except when specifically mentioned.

TABLE 4.—*Forty-Three False Reactors Encountered in 263 Cases of Vaccinia*

	±	+	++	+++	++++	Total
Kline	6	7	0	0	1	14
Kolmer	0	1	1	0	5	7
Hinton	13	6	11	0	1	31
Mazzini	11	7	4	4	2	28
Total	30	21	16	4	9	80
Number of persons in whom this was the highest reaction	14	12	9	2	6	43 (16%)

Of the 263 persons giving no reactions before vaccination, 43 (16 per cent) reacted to one or more of the subsequent tests; 23 (9 per cent) reacted to more than one of the standard serologic procedures. When reactions to all four tests (Kolmer, Kline, Hinton and Mazzini) are considered, a total of eighty positive and doubtful reactions were obtained. Table 4 shows the number and distribution of these reactions.

In the majority of instances the strongest reaction was doubtful or weakly positive; fifty-one of the total of eighty reactions were only ± or 1 +; in 26 of the 43 persons the strongest reaction was ± or 1 +. Four plus reactions to any of the tests were reported for only 6 of the 263 persons studied (2.3 per cent). Two plus or stronger reactions were reported on specimens from 17 persons (6.5 per cent).

TABLE 5.—*Three Cases in Which False Strongly Positive Serologic Reactions Were Obtained on Single Specimens*

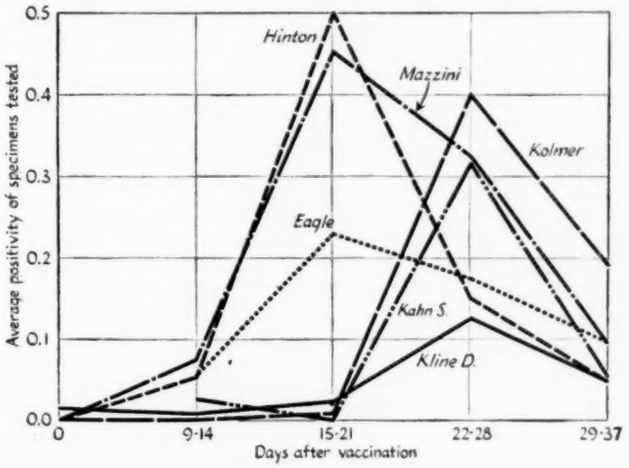
	9/24	10/10	10/24	11/19
Kline	—	—	±	—
Kolmer	—	—	4+	—
Hinton	—	—	—	—
Mazzini	—	±	3+	—
Eagle	..	—	—	—
Kahn	..	—	3+	..

	9/23	10/7	10/24	1/8	3/6
Kline	—	—	1+	1+	1+
Kolmer	—	—	4+	—	—
Hinton	—	—	—	—	—
Mazzini	—	—	3+	—	—
Eagle	..	—	3+	—	—
Kahn	..	—	3+	—	..

	9/27	10/23	1/23
Kline	—	2+	—
Kolmer	—	4+	—
Hinton	—	2+	—
Mazzini	—	4+	—
Eagle	..	3+	—
Kahn	..	2+	—

Among the various tests there was considerable difference in the incidence of the false positive reactions following vaccinia. Under the conditions of this study, the Kolmer test was the most specific, since positive reactions were obtained in only 7 persons, but 4 + reactions were noted in 5 of this group. There were 13 ± or 1 + reactors to the Kline test but only 1 with a stronger reaction. The Hinton and Mazzini tests gave doubtful or positive reactions in 31 and 28 persons respectively. Because the Eagle and Kahn tests were not performed on all specimens, the relative incidence of false positive reactions cannot be determined exactly, though in each case it appears to be intermediate between that of the Kline and that of the Mazzini test. It is interesting to note that all six technics gave this type of false positive reaction to some degree. In several cases strong reactions were given by most of the technics used; such reports might have presented diagnostic problems to the clinician had the specimen been collected as a part of a routine physical examination.

Of the 4 cases in which the diagnostic Kline test gave a reaction before vaccination, 1 showed no reaction to the Kline test after vaccination, though the Mazzini reaction was ±. In a second case (1 +) the reaction after vaccination was the same, but in addition a doubtful reaction to the Hinton test was reported. In the remaining 2 cases the Kline reaction was stronger after vaccination, in 1 (±) it became 1 +, and in the other Mazzini 1 + and the Hinton and Eagle were each ±. (2 +) it became 4 +, the Kolmer became 2 +, the



Average positivity of reaction to serologic tests for syphilis on the first postvaccination specimen of 271 persons.

Although it was suggested that specimens be collected from twelve to fourteen days after inoculation, not all the patients submitted exactly to this routine and in many cases the first test was performed much later. An attempt has been made to analyze the data so as to determine the incidence of false positive reactions to the various tests with respect to the time interval following vaccination. When the first specimen was submitted from fifteen to twenty-one days after vaccination, positive reactions were more common with the Hinton, Mazzini and Eagle tests. On specimens on which the first test was performed from twenty-two to twenty-eight days after inoculation the Kolmer, Kahn and Kline tests were more likely to give a positive reaction, as shown in the accompanying chart.

The reactions remained positive for as long as two months in many of the persons tested; in a few the reactions were still positive after four months. One (Kline 1 +) was still present at one hundred and sixty-four days; in this case reactions with the Kolmer, Kahn,

Eagle and Mazzini tests had been positive at thirty-one days but were negative at one hundred and seven days and again at one hundred and sixty-four days.

The Kahn verification test was performed on the serum of 1 person who has not previously been mentioned in this report because he was in a smaller group studied several months later. On a specimen collected at the time of vaccination and another collected twenty-four days later the Kline diagnostic, Kolmer Wassermann, Hinton and Kahn tests gave negative reactions. A third specimen collected forty-three days after vaccination gave the following reactions: Kline diagnostic 2+, Kolmer Wassermann negative, Hinton 2+, Kahn 3+. A fourth specimen collected forty-seven days after vaccination gave the following reactions: Kline diagnostic doubtful 1+, Kolmer Wassermann negative, Hinton 3+, Kahn doubtful 1+. Kahn verification tests performed on the latter 2 specimens gave "the syphilitic type" reaction. It might be well to recall here that Kahn has pointed out that, while a negative verification test is strongly suggestive of the absence of syphilis, "there are no data available which establish that a positive verification reaction means syphilis in every instance." [9]

COMMENT

The incidence of false positive serologic reactions following vaccinia might have been determined more accurately had this survey been conducted in a different manner. The study served its initial purpose, which was to determine whether such reactions occur. Bay and Sankstone had stated that their number must be less than 1 per cent, but we found false doubtful or positive reactions in 16 per cent of 263 persons studied after primary vaccinia.

Such reactions may be strongly positive and may therefore be a source of confusion to the clinician. They may persist for several months after vaccination. Testing by multiple methods increases the recognized number of positive reactors, as shown by the fact that each of six standard diagnostic technics resulted in this type of false positive reaction. The different tests usually gave varying degrees of reaction; rarely were all tests positive on the same specimen. In the only case in this series in which the Kahn verification test was performed the reaction was of the syphilitic type; Thomas and Garrity [6] had a similar experience.

Many of the persons in this series were tested only once after vaccination, and it is now known that this test was performed too early to have all the false reactors recognized. The maximum height of positivity was not always recorded at the first test, and it is likely that tests performed on a greater number of specimens would have led to recognition of additional positive reactors among those persons whose first postvaccination test was negative to even the Kline exclusion test.

The data submitted in this report suggest that recognition of the highest possible number of false positive reactions would require the performance of tests on specimens collected more frequently through the period from two to six weeks after vaccination. If this procedure had been followed, the incidence of false reactions would probably have been quite different, and there might also have been a difference in the relative number of false reactions demonstrated by the different diagnostic technics.

9. Kahn, Reuben L.: A Serologic Verification Test in the Diagnosis of Latent Syphilis, Arch. Dermat. & Syph. **41**: 817, 1940.

ABSTRACT OF DISCUSSION

DR. FRANCIS E. SENEAR, Chicago: Dr. Lynch and his co-workers have presented a careful study of the effect of vaccination in the production of such reactions and, though the first mention of this was made in the literature only last year, make it apparent that vaccinia must be added to the list of conditions capable of producing a false positive reaction for syphilis. Apparently these false positive reactions due to vaccinia follow the pattern of those evoked by some other disorders, a pattern which should always arouse suspicion as to the source of the positive finding. Such reactions are apt to be weakly positive, vary in intensity with different tests or with the same test in different laboratories and show fluctuation in titer from day to day with the same test performed in the same laboratory. In this particular disease it would seem as though we have available a condition which offers great possibilities for study of these biologic false positive reactions, because in the other diseases in which such reactions are obtained we never know whether the patient is to have them or not; we are often uncertain as to the qualification of the laboratory performing previous tests, if we can find that they have been performed previously. But with a disorder of this type, in which, if, as Dr. Lynch and his co-workers' figures show, 16 or 32 per cent of the patients will develop some degree of positive reaction, in which one can check the state of the reaction before the vaccination is performed, it seems to me there is an opportunity for very extended study. One can hardly say yet that the verification reactions, such as Witebsky's or the Kahn verification, can solve this problem. I see Dr. Kline sitting over here and I have no doubt that he will be able to say something about the implications presented by these changes in association with vaccinia. The authors are to be congratulated on having made available so quickly some definite information as to the effect of the commonplace procedure of vaccination in giving rise to false positive reactions for syphilis for temporary, though sometimes prolonged, periods. I would like to speak of the apparently greater specificity in this study of the Kolmer complement fixation reaction. This observation would further support the view held by many observers that, when two or more tests are to be used jointly, one of them should be of a complement fixation type.

DR. B. S. KLINE, Cleveland: Nonspecific reactions in tests for syphilis are easier to explain than are the specific reactions. In every laboratory, even the practicing physician's small laboratory, there are many things which will flocculate the antigen particles in the emulsions used for the detection of syphilitic reagin. These lipoid particles have certain physicochemical properties that permit them to be flocculated by dehydrating agents like alcohol and by various electrolytes, including acids and ordinary salts. It is remarkable therefore that these emulsions may be used successfully in the detection of syphilis. Before a false positive test is regarded as a biologic reaction, it is the duty of the serologist to make sure that the reaction is not caused by adventitious material in the antigen. Plain alcoholic extract antigens, for instance, contain so much adventitious material that causes so many nonspecific reactions that they are no longer used in the serodiagnosis of syphilis. Furthermore, my associates and I discontinued the use of Kahn antigen dilution some years ago because in tests at low temperature it gave nonspecific reactions in too great number. Subsequently Kahn antigen was found to contain either insoluble or water soluble impurities. Satisfactory results with this indicator, it was found over ten years ago, can be obtained only at a temperature of 70 F. or over. We have found that even carefully prepared slide test antigen contains impurities that may be removed by extraction with water. At Western Reserve University Dr. Wellman and Dr. Lankelma are making a chemical study of antigens. In another few years they will find a way of isolating the most potent and most specific substance in heart powder in pure form, and then all the headaches for the serologists and a great many for the dermatologists and syphilologists will be eliminated. The use of purified antigens, however, doesn't mean that in malaria and leprosy and in lower animals there won't be a great many nonspecific reactions. As far as testing animal serums is concerned, it should be remembered that the majority of untreated serums of syphilitic

individuals give no reactions with antigen emulsions. The serums must first be heated or there is no reaction. Another way to increase the flocculating capacity of serum is to add a small quantity of electrolyte, such as sodium chloride, in the proper concentration. Horse serum contains more abundant electrolytes apparently than human serum, and because of this there is no more reason for dragging in horse serum to test its ability to flocculate antigen emulsions than for taking calcium chloride or other electrolyte out of a bottle to test its action on antigen emulsions. In leprosy and malaria it may be found that some chemical substance other than reagin is produced in excess and that it thereby causes the flocculation of the antigen particles.

DR. ADOLPH B. LOVEMAN, Louisville, Ky.: Dr. Lynch and his co-workers have rendered a great service to the dermatologists in calling attention to the false positive reactions following vaccination. About four months ago, I saw my first case, in a nurse. In this particular case the Kahn, Kline diagnostic and Kline exclusive tests were all positive but the Kolmer Wassermann test was negative. This was repeated in several laboratories. The Wassermann test in this particular case never became positive. About three months later a soldier came in on a Friday and wished to be married the next day. He also had a positive Kahn, Kline diagnostic and Kline exclusive test and a negative Kolmer Wassermann test. This likewise was repeated in several laboratories. At that time I was suspicious that it was a postvaccinial reaction and we sent the test to Dr. Kahn for his verification test, who reported a biologic type of reaction. This case was rather dramatic in that all tests including a reply from Dr. Kahn were completed in twenty-four hours and the soldier got married according to schedule. These are important cases. In the few selected cases in which repeated tests were made following vaccination for recurrent herpes, in which there were no takes, I did not get any positive reactions from the Kahn, Kline or Wassermann tests.

DR. CHARLES R. REIN, New York: I agree with Dr. Kline that many of the false positive serologic reactions are of the technical type and that a considerable number of these technical false positives will be eliminated with the purification of the antigens. There are, however, a number of diseases and conditions which may produce transient and even permanent biologic false positive reactions. Dr. Lynch and his collaborators have shown today that such false positive reactions may develop following smallpox vaccination. I have encountered many biologic false positive reactions immediately following acute upper respiratory infections. The blood of these patients, however, usually becomes negative in three to four months. Dr. Chargin and I found but few false positive reactions in a group of 119 patients with varicella, scarlet fever and measles, in whom the temperature ranged up to 105 F. The clinician must be aware of the fact that biologic false positive reactions may occur and he must be on the lookout for them. Unquestionably, many a person has been stigmatized as syphilitic and indeed given treatment purely on the basis of a positive test occurring in routine examination in the course of or immediately following a nonsyphilitic disease.

DR. ARTHUR G. SCHOCH, Dallas, Texas: I would like to ask whether or not in the group of supposedly syphilitic persons the authors established that diagnosis on the basis of serologic results alone? If so, what type of serologic reaction did they consider of such little significance that it was not indicative of true syphilitic infection? Did they do any quantitative determinations? I think we are quibbling when we start differentiating between what constitutes a biologic false positive and a technical false positive reaction and possibly false positive reactions in animals. They are false, and as they are reported to us they are positive. There is a clerical false positive reaction which can be cleared up by merely repeating the test in the same laboratory. Clerical false positive reactions do occur and I would just like to call attention to the fact that sometimes they get the wrong number on the right tube.

DR. FRANCIS W. LYNCH, St. Paul: In reply to Dr. Schoch's question, these are the criteria which we have applied in the diagnosis of syphilis in college students. If they are observed strictly, there is little danger of false diagnosis based on serologic reactions such as we reported today; nevertheless, we believe it worth while to try to demonstrate the cause of every false positive or doubtful reaction. Another question by Dr. Schoch suggested the possible value of applying quantitative studies when dealing with questionable serums. We are unable to report any experience with quantitative tests. Dr. Kline's discussion emphasized the newer technical knowledge which can be applied to prevent or minimize the number of false reactions. Such details are particularly of importance to the serologist. It is only by further recognition of these and similar facts that serologic reports can become more dependable. Yet the clinical syphilologist must of necessity accept the report which is given to him. His primary concern is not the determination of the cause of the falsity but rather the absence or presence of syphilis. Dr. Loveman mentioned two previously unreported cases of false reactions associated with vaccinia. Other clinicians must have had similar experiences but have probably thought that the incidence of such an occurrence was much less than our studies suggest. We have not critically analyzed the reports of serologic studies following immune reactions to vaccinia, but in several instances we have noted doubtful or weakly positive reactions. Dr. Rein mentioned the association between false positive reactions and upper respiratory infections, a point which is also demonstrated in a report by Clifton and Heinz (THE JOURNAL, May 4, 1940, p. 1731). It is likely that false reactions accompany many febrile diseases to a much greater extent than has previously been realized.

SOME THERAPEUTIC EXPERIENCES WITH HODGKIN'S DISEASE

OVID O. MEYER, M.D.
MADISON, WIS.

The cause of Hodgkin's disease remains obscure, but the theories of the causative factors are well known. The possible significance of the recent reports of Wise and Poston,[1] who have demonstrated the frequent presence of Brucella melitensis in the lymph nodes of patients with lymphogranulomatosis, is yet to be established. These workers have analyzed their results with commendable objectivity and without ascribing a final etiologic relationship to these organisms. Dr. E. A. Birge [2] has cultured specimens from the lymph nodes of 10 patients with Hodgkin's disease seen at the Wisconsin General Hospital but has been unable to demonstrate Brucella organisms. It should be observed, however, that brucellosis is much less common in Wisconsin than in the regions where the patients of Wise and Poston [1] live. This factor has already been weighed by these observers, and further discussion of it is unnecessary.

The therapy of Hodgkin's disease is fairly well standardized at present. It is generally agreed that roentgen ray or radium therapy is indicated in practically all cases. Some authors (Desjardins,[3] Jacox, Pierce and Hildreth [4]) advocate early irradiation of all sites of lymph nodes. Others, the majority, prefer to direct treatment only to areas where disease appears. All are in essential agreement that the therapy is merely a palliative except in rare cases and that therefore the aim should be to alleviate symptoms and, if possible,

From the Department of Medicine, University of Wisconsin Medical School.

Read before the Section on the Practice of Medicine at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

1. Wise, N. B., and Poston, Mary A.: The Coexistence of Brucella Infection and Hodgkin's Disease, J. A. M. A. **115**: 1976-1984 (Dec. 7) 1940.
2. Birge, E. A.: Personal communication to the author.
3. Desjardins, A. U.: Radiotherapy for Hodgkin's Disease and Lymphosarcoma, J. A. M. A. **99**: 1231-1236 (Oct. 8) 1932.
4. Jacox, H. W.; Pierce, C. B., and Hildreth, R. C.: Roentgenologic Considerations of Lymphoblastoma, Am. J. Roentgenol. **36**: 165-168 (Aug.) 1936.

prolong life. It appears that relief of symptoms is about as satisfactory—and often it is highly satisfactory—when only one or more of the involved areas is treated as when extensive irradiation is employed.

It is not my purpose here, however, to argue for one or the other method of management or to analyze treatment in a series of cases for the purpose of establishing the value of roentgen therapy. Rather, I wish to cite some experiences we have had in order to point out certain lessons learned therefrom: to demonstrate some of the hazards that attend irradiation, to indicate some of the complications that patients experience without apparent untoward effects, to demonstrate the favorable results that may follow properly controlled roentgen therapy and, finally, to urge a more optimistic attitude toward the individual patient, for there is no known prognostic guide which is completely reliable in any given case. Although the average duration of the disease is about three years, neither the patient's age nor sex, the extent of the disease, the status of the blood nor the roentgenographic findings will indicate the expectancy of comfortable life. Hence the physician is justified in taking a more optimistic view in his dealings with the individual patient than he usually does at present.

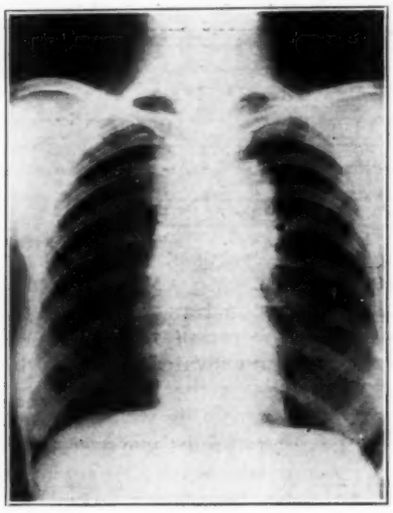


Fig. 1.—Appearance of the chest of patient M. K. at the time of first admission.

Fig. 2.—Appearance of M. K.'s chest after irradiation of the mediastinum, demonstrating atelectasis of the right lung.

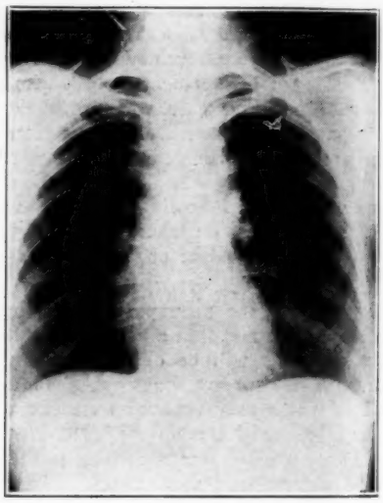


Fig. 3.—Appearance of M. K.'s chest Feb. 1, 1939, two months after therapy.

REPORT OF CASES

CASE 1.—Mrs. M. K., a housewife aged 29 who had been a registered nurse, was admitted to the hospital in November 1938. In May 1937, while pregnant, she had a pain in the chest just behind the sternum. After the birth of her child in September, the pain became worse. Subsequently it subsided, but five weeks before admission she had shortness of breath. As this progressed, a productive cough developed. A roentgenogram of the chest showed widening of the mediastinum. The menses had ceased again four months before she came under my observation.

Physical examination showed the patient to be well developed, undernourished and rather uncomfortable and to have slight cyanosis, cough and, on slight exertion, severe dyspnea. The veins of the neck were distended. There were signs of a mediastinal mass, but there was no enlargement of the superficial lymph nodes. Pelvic examination revealed enlargement of the uterus to the size produced by a 3 or 4 month pregnancy.

The blood showed a hemoglobin content of 10.6 Gm., 3,620,000 erythrocytes and 20,700 leukocytes, with 92 per cent neutrophils. An Aschheim-Zondek test gave positive results. Roentgenograms of the chest showed a mass of soft tissue projecting from each side at the level of the aortic arch. There was some compression of the trachea near the bifurcation.

Irradiation of the mediastinum was decided on although no lymph node was available for biopsy. After being given two small doses of 100 r each to the anterior and the posterior mediastinum on successive days, the patient had severe dyspnea and signs of complete atelectasis of the right lung. She was unimproved for four days and then began to cough violently, raising much mucus, and the lung reexpanded. Therapy was then resumed, and eight more treatments were given without untoward effects.

On Feb. 1, 1939 a roentgenogram of the chest showed definite shrinkage of the mediastinal mass and there was subjective improvement. Two months later she was readmitted with the complaint of recurrence of difficulty in breathing. Since her admission of 1938 she had had tenderness and enlargement of the lymph nodes in the right axilla and the right side of the neck. Biopsy of a supraclavicular node showed endothelial proliferation, many Sternberg-Reed cells and eosinophils and diffuse infiltration by polymorphonuclear leukocytes. There was frank pus about the node, from which diphtheroid organisms grew on culture. A roentgenogram of the chest showed that the mediastinum had become enlarged to approximately its former size.

Another course of roentgen therapy was started. After three treatments of 150 r to the anterior and the posterior mediastinum given over four days, signs of atelectasis of the middle and lower lobes of the right lung developed. A thick, gummy material was aspirated with a bronchoscope. The patient was then able to complete the total course of thirteen treatments uneventfully.

In May 1939 the patient was delivered of a normal child. In June she returned to the hospital and received roentgen therapy to the mediastinum and the right axilla. In October she returned once more, with signs of nearly complete atelectasis of the right lung. The mediastinal mass was not especially large, but further therapy was given. Apparently immediately thereafter, the patient became pregnant for the third time, and in January 1940 a therapeutic abortion was performed.

Subsequently, she was admitted to the hospital on four occasions. Atelectasis of the right lung persisted. At one time peribronchial fibrosis of the left lung was demonstrated. Fluid accumulated in the right pleural cavity from time to time. Ascites developed, and paracentesis was required. Considerable deformity of the chest, with scoliosis, appeared.

The patient's final admission to the hospital occurred in February 1941. She had lost weight and was pale and had anasarca. There was gross enlargement of a left supraclavicular node. The atelectasis of the right lung continued, and a roent-

genogram of the chest showed a well defined, rounded rarefaction about 4 cm. in diameter just below the level of the left clavicle. The patient died on February 19.

Postmortem examination revealed no disease of the lymph nodes except in the mediastinum. All bacteriologic studies, including search for tubercle bacilli, gave negative results. There was extensive fibrosis of the right lung, with fibrosis about the large vessels, which showed endarteritis. These changes had produced an increased load on the heart, and chronic cor pulmonale resulted. The cavity in the left lung showed a wall of granulation tissue about an abscess. In the wall there were many atypical reticuloendothelial cells.

COMMENT

This case demonstrates several points. The patient had three pregnancies, of which two went to term, during the course of her illness. It was not demonstrable that they affected the illness favorably or unfavorably. One does not, of course, know what the outcome would have been had the pregnancies not existed, but the duration of illness was about forty-five months, which is as long as the average.

CASE 2.—Mrs. H. J., a housewife aged 40, was referred on July 25, 1940 to the Wisconsin General Hospital from a sanatorium where a diagnosis of pulmonary tuberculosis and exfoliative dermatitis had been made. Previously she had had pruritic lesions on the forearms and the scalp, had fatigued easily and had experienced night sweats and pain in the right part of the thorax due to pleurisy. She was sent to us because of the troublesome condition of the skin. There was no history of contact with tuberculosis.

Physical examination revealed emaciation and a severe generalized dermatitis involving the scalp particularly. There was generalized erythema, with thickening and scaling and bullous lesions on the fingers. There were signs suggesting infiltration at the apex of the right lung. Enlarged lymph nodes were noted in the cervical, inguinal and epitrochlear regions, the largest less than 2 cm. in diameter. The liver was palpable; the spleen was not palpated.

Laboratory studies revealed a hemoglobin content of 11.1 Gm.; 5,330,000 erythrocytes and 10,600 leukocytes, with 80 per cent neutrophils, 3 per cent monocytes, 8 per cent lymphocytes, 8 per cent eosinophils and 1 per cent basophils. Many examinations of the sputum and the gastric contents were negative for tubercle bacilli, and inoculated guinea pigs remained normal. Examinations were negative for fungi. A stereoscopic roentgenogram of the chest showed a conglomerate opacity at the periphery of the fourth interspace laterally and some rather isolated areas of nodular infiltration in the midportions and in the lower part of the right lung field. On the left there was a somewhat homogeneous opacity extending from the first interspace anteriorly to the level of the fifth rib. There was pleural thickening peripherally in the lower half of the left lung field. A roentgenographic study of progress on September 7 showed that the condition had cleared in some areas and had extended in others. Bronchoscopic study at this time revealed no abnormality.

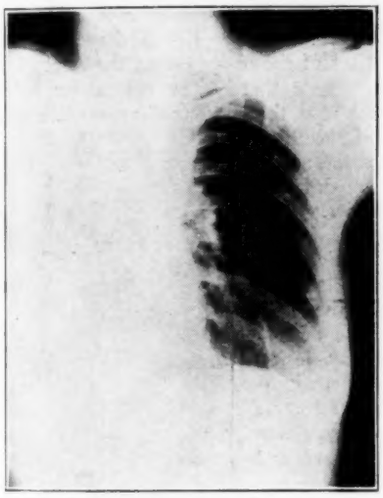


Fig. 4.—Appearance of M. K.'s chest in December 1939, when atelectasis had become permanent.

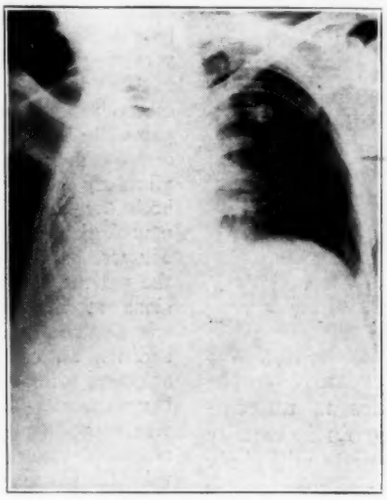


Fig. 5.—Appearance of M. K.'s chest eight days before death. There are definite thoracic scoliosis, persistence of atelectasis and a cavity in the left infraclavicular region close to the sternum.

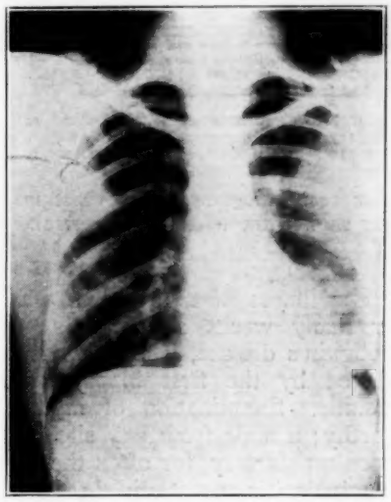


Fig. 6.—Appearance of H. J.'s chest at the time of first admission, July 1940.

The production of atelectasis after irradiation of the mediastinal masses is a hazard that must always be considered. It is supposedly due to reaction and swelling of the mass, with bronchial compression. Furthermore, there may be bronchial reaction and hypersecretion. Actually, however, atelectasis is not common, and it is rather astonishing that in the foregoing case small doses cautiously applied repeatedly produced it. When mediastinal lymphomatous masses exist, the possibility of beginning therapy at a distant site or with general irradiation should perhaps be considered.

Finally, the pathologic changes are of interest. The cavitation appears to be a result of actual infiltration of the lung with the tissue of Hodgkin's disease, with perhaps a secondary factor of infection. It is well recognized that pulmonary involvement occurs in Hodgkin's disease. The additional grosser findings of extensive fibrosis and endarteritis, which were, at least in large part, a result of intensive irradiation, the total dose over the two years being large, with resultant chronic cor pulmonale, emphasize another hazard of irradiation to the mediastinum and the lungs.

It was established that the dermatitis was due to contact with a proprietary hair lotion containing marrow oil. This lesion cleared with local applications and the avoidance of contact with oils. Some months later a patch test with the marrow oil of the shampoo produced a violent reaction.

An inguinal lymph node was removed on August 22, and microscopic study of this revealed chronic hyperplastic lymphadenitis.

Since the pulmonary lesions persisted and no explanation for them was available, an epitrochlear node was excised and examined microscopically. This showed scarring, some loss of structure, eosinophils, endothelial proliferation and Sternberg-

Reed cells. Dr. C. H. Bunting and Dr. W. D. Stovall agreed that the changes were those of Hodgkin's disease.

The patient was then given ten treatments of 150 r each to the anterior and the posterior part of the right lung alone over the twelve days between September 26 and October 7. The total dose was 3,000 r. A roentgenogram taken on October 8 showed a clearing of the infiltrative change in both lung fields. Only a few small areas remained in each lung. The patient was again seen on November 7. She had felt well in the interval and had gained 15 pounds (6.8 Kg.). A few scattered superficial nodes were palpable. Roentgenograms showed that the lungs were still clear save for a few small infiltrations. The superior mediastinal shadow had broadened slightly, particularly on the right. It was decided not to irradiate at this time, and the patient was discharged. She has remained well, and another roentgenogram of the chest made in February of this year showed the lungs to be normal.

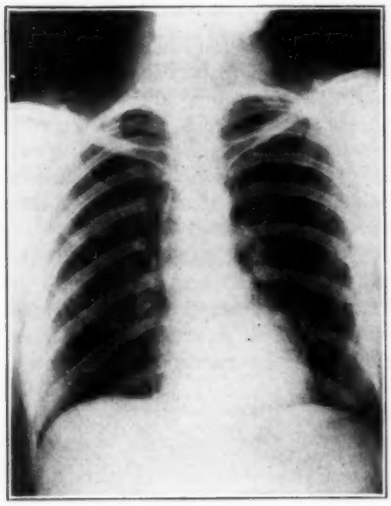


Fig. 7.—Appearance of H. J.'s chest in February 1941. A roentgenogram in October 1940 had shown a similar degree of clearing.

COMMENT

The illness of this patient was a diagnostic puzzle for many weeks after admission. The suspicion of Hodgkin's disease, which was slow in developing, was allayed by the first biopsy, which revealed lymphadenitis. Examination of inguinal nodes is untrustworthy; a node from any site but the groin is usually more satisfactory, for often the inguinal node will show lymphadenitis, as it did in this case, whereas nodes from other sites will be affected by the primary disease.

Hodgkin's disease, in the opinion of Piney,[5] is a disease of the reticuloendothelial system. Hence manifestations of the disease may predominate at any of several sites, including the lungs. One must recognize that intrathoracic involvement may be of many types other than disease of the mediastinal lymph nodes.

Moolten[6] has discussed the subject at length and has recorded the many changes, infiltrative, miliary and pneumonic, as well as invasion from mediastinal lymph nodes, that may occur. Versé[7] has stated that in about 10 per cent of cases of Hodgkin's disease of the lung the primary lesion is pulmonary.

The response to irradiation in case 2 was striking and gratifying. Possibly it was overconservative to limit irradiation to one lung, but no disadvantage could result from this caution, and the response in the two lungs was not completely unexpected in view of the diagnosis, since occasionally one sees an effect of treatment at a distance from the primary site of irradiation in cases of lymphoblastoma. Unquestionably a certain amount of scattered radiation reached the left lung.

5. Piney, Alfred: Endotheliomas with Especial Reference to Those Growing in Compact Form, Arch. Path. **2**: 301-317 (Sept.) 1926.

6. Moolten, S. E.: Hodgkin's Disease of the Lung, Am. J. Cancer **21**: 253-294 (June) 1934.

7. Versé, M.: Die Lymphogranulomatose der Lunge und des Brustfells, in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, vol. 3, 3, 1926.

CASE 3.—E. K., a boy aged 14 who had played football on his high school team, was admitted to the hospital on Nov. 26, 1940. In 1933 he had noticed a progressive painless enlargement of lymph nodes in his neck. A biopsy was done, a diagnosis of Hodgkin's disease was made and roentgen therapy was instituted, with prompt disappearance of the masses. Thereafter he had treatments when necessary. In July 1940 he had pains in the back and in the calves of the legs which rapidly became more severe and were stabbing on movement of the hips. Weakness in the lower extremities became severe, and from July until admission the patient had been bedridden. His physicians were pessimistic regarding his condition, and only symptomatic therapy was instituted.

Physical examination revealed that the patient was uncomfortable, pallid and bedridden, with firm, nontender, discrete, movable nodes, up to 5 cm. in diameter, in the left cervical region. The spleen and the liver were palpable below the costal margin. There was weakness of the legs, especially of the flexors and the abductors of the thigh, the extensors of the leg, and the dorsal and plantar flexors of the feet and toes. The knee jerk and achilles tendon reflexes were exaggerated, and there was bilateral ankle and patellar clonus. The Babinski reflex was present, and confirmatory tests gave positive results. The muscles of the calves were somewhat atrophic. The sensory picture was bizarre, with widespread hypesthesia, slight at the level of the eighth dorsal vertebra persisting to the lower part of the abdomen, at the level of the twelfth dorsal vertebra, where there were normal or hyperesthetic reactions. In the legs the sensory changes took place primarily at the levels of the third and fourth lumbar vertebrae. The vibratory sense was impaired in both the lower extremities. The neurologic consultant, Dr. M. J. Musser, expressed the belief that the patient had intramedullary lesions at the levels of the fifth and sixth dorsal vertebrae and in addition an extramedullary lesion affecting primarily the fourth lumbar vertebra. Motion of the spine was limited by pain, and there was a gibbus between the second and third lumbar vertebrae.

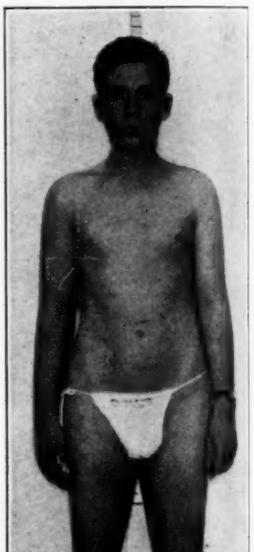


Fig. 8.—E. K. four months after completion of roentgen therapy to the spine and cord.

The blood showed a hemoglobin content of 12.2 Gm., 4,690,000 erythrocytes and 13,200 leukocytes, with 74 per cent neutrophils. A roentgenogram of the spine showed an early sclerotic density of the body of the second and sixth dorsal vertebrae. There were a distinct gibbus at the level of the third lumbar vertebra and minimal changes in the body of this vertebra. A roentgenogram of the chest showed a slight increase in the mediastinal shadow indicative of enlargement of lymph nodes.

The patient received six treatments of 200 r each to the dorsal and lumbar portion of the spine. Before his discharge from the hospital on December 12 most of the pain in the back had subsided and some muscular power had been regained.

Two months later he returned to the outpatient department. All pain had subsided, he had gained about 20 pounds (9.1 Kg.) and he was up and about on crutches. The liver and the spleen were no longer palpable, and there was no enlargement of lymph nodes. There was no spinal tenderness. Reflexes were still hyperactive in the lower extremities, and there was a Babinski reflex on the left. Minimal sensory changes and impairment of the vibratory sense persisted below the knees.

The hemoglobin content was 15 Gm. and the erythrocyte count 4,170,000. No treatment was advised, and the patient returned home.

He came to the outpatient department again on April 2, walking with a wide base, without crutches. He had gained 17 pounds (7.7 Kg.) and now weighed 153 pounds (69.4 Kg.). Deep tendon reflexes were about normal; the Babinski reflex

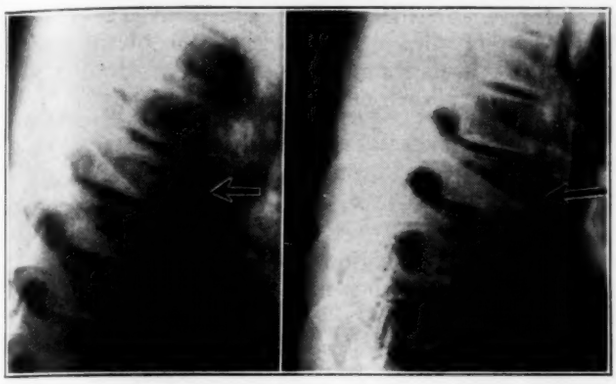


Fig. 9.—The sixth dorsal vertebra of E. K., before and after irradiation.

was present bilaterally. There was no enlargement either of lymph nodes or of the spleen. The liver was just palpable. Roentgenograms of the spine showed a return to normal of the appearance of the vertebrae. The blood count was essentially normal.

COMMENT

Case 3 emphasizes the striking improvement that may follow irradiation of the spine when lesions of the spinal cord exist. Vertebral lesions in Hodgkin's disease are common. If treatment is not vigorously instituted, compression fracture and paralysis may result. In this case there was nothing to suggest that this had occurred, but disease of the spinal cord existed as a result of lymphogranulomatous involvement. Lesions of the cord are not rare; often laminectomy has been done and tissue removed surgically. This procedure is ordinarily unnecessary, especially if proper treatment is instituted early. Fortunately it was possible to repair the damage in case 3.

This case also emphasizes how difficult the prognosis of Hodgkin's disease is and how improper is an attitude of complete pessimism. The boy had Hodgkin's disease first when he was 7. The consensus is that children and young adults are more likely to have a shorter span of life than those who develop the disease at later ages. But one cannot say that this will be true in any specific case. Further, even though, as is not infrequently the case, involvement of the vertebrae and the cord is likely to be a late manifestation of the disease, the laissez-faire attitude is not justifiable. With only a modicum of roentgen therapy patient 3 has already had months [8] of freedom from pain, and he is up and about after previous months of unnecessary pain and the restrictions of a bedridden invalid.

CONCLUSION

No doubt almost every one who treats Hodgkin's disease could duplicate experiences such as those I have set down, each of which furnishes its lesson. In emphasizing the hazards and the desirability of greater optimism I have had no intention of minimizing the importance of continued search for the cause of Hodgkin's disease and better therapeutic measures or cure.

8. This patient was seen again July 24, and he is still well. He has received no irradiation since December 1940.

ABSTRACT OF DISCUSSION

DR. RAPHAEL ISAACS, Chicago: Dr. Meyer has chosen his patients well in order to illustrate certain points. A problem which comes up frequently is the question of Hodgkin's disease and pregnancy, and the question also of pregnancy and roentgen treatment. The patient described by Dr. Meyer received thirteen roentgen treatments while she was pregnant. I judge this would amount to almost 2,000 roentgens given to the patient during pregnancy, and presumably a normal child was born. That point is important, because there is much in the literature to make one worry about whether roentgen rays will affect the child or not. The second point is that the literature seems to indicate that Hodgkin's disease is aggravated by pregnancy. However, this patient appeared to go through pregnancy without any immediate exacerbation of the disease. Dr. Meyer points out the presence of Hodgkin's lesions in the lungs and the danger of atelectasis. The involvement of the bone and its dramatic improvement with roentgen therapy I can confirm with patients in my own experience, and the outlook sometimes is good. Pregnancy during Hodgkin's disease is quite different from pregnancy and lymphosarcoma. Lymphosarcoma may recede during pregnancy, with apparent disappearance of all signs of the disease. The lymph glands may become normal in size, but they enlarge again after the baby is born. What does one do to Hodgkin's tissue when one gives roentgen treatment? Presumably one decreases the number of lymphocytes in the Hodgkin's glands without gross effect on fibrous tissue. Fibrous tissue is the type of tissue which forms the bulk of the large glands. This is an important point to remember in trying to reduce a gland to normal size. It is felt that Hodgkin's disease is more of an infection than a neoplastic disease, and for that reason the future is looked forward to to more hopeful prognosis. Hodgkin's disease is twice as frequent in males as in females, and this will, I think, furnish a clue to treatment in the future. The characteristics of Hodgkin's tissue as it invades other tissue is not like a neoplastic cell invading tissue, but it resembles what would happen if the invaded tissue had become infected.

DR. W. EDWARD CHAMBERLIN, Philadelphia: Dr. Meyer is right in pointing out that we learn about Hodgkin's disease by these individual cases. His 3 cases illustrate very different types of Hodgkin's disease and very different responses to therapy. I suppose the reason the manifestations of Hodgkin's disease are so protean is that it is a disease of the reticuloendothelial tissue, which, after all, is found in most of the organs of the body. Cases have been seen in which the disease simulated Riedel's struma. Even the surgical pathologist, looking at tissue removed for clinical diagnosis, agreed that the tissue was probably Riedel's struma, but we found later on it was Hodgkin's disease primary in the thyroid gland. I had a case that simulated scabies for a long time. The patient was over a year in the skin clinic with itching of the skin. There were no glandular masses anywhere and it was thought to be scabies because of the intense itching. It turned out to be Hodgkin's disease and manifested itself in the thorax and peripheral lymph nodes. There is a great deal of difference in the roentgen ray diagnostic aspects of primary Hodgkin's disease in the lung and in the mediastinum. In the mediastinum a typical smoothly outlined, apparently encapsulated mass is seen, while, if the lung is involved, finger-like infiltration is noted in the lung tissue. I saw a case in which it simulated breast cancer in a woman aged 37 because it was not believed that the mass in the axilla came before the mass in the breast. Occasionally there are cases in which there are no masses at all. There was such a case at Stanford about fifteen years ago. Patients die with various diagnoses when really the condition is Hodgkin's disease. There are many diagnoses missed. One has to be more on the lookout for Hodgkin's disease. The diagnosis is not going to be made unless one remembers that it is one of the possibilities in these cases with such remarkable protean manifestations. I think Dr. Meyer is close to the secret of success in treatment, but I think he has to go a step further. He is willing to let a patient go without treatment at times, and I think that is important. One rule is important in the management

of Hodgkin's disease. We are only palliating; we are not curing, and therefore we must try to make it definitely palliative. Big doses sometimes make the patient feel miserable, and remarkable results can be obtained with minute doses. I have given as little as 20 roentgens to a lesion and have seen it regress. The rule is this: Try to get along with the smallest possible individual and total dose that will keep the patient comfortable.

CANCER OF THE LOWER LIP

TREATMENT WITH RADIATION

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The choice of treatment for cancer of the lower lip varies widely in the different medical centers where large numbers of patients with this condition are seen. Physicians who attempted the use of radium and roentgen rays with inadequate doses in the early periods of these forms of therapy immediately turned to more satisfactory means of treating malignant lesions by actual cauterization and plastic surgical operations. These methods have been carefully developed, and their application is successful in producing cures.[1] Equally successful has been the use of irradiation by roentgen rays and radium when employed in sufficient doses.[2]

In our hands, the most successful treatment for cancer of the lip has been a combination of the gamma rays of radium with unfiltered or lightly filtered roentgen rays. This will provide an adequate dose by treatment on successive days to effect a total, continuous or massive dose, which is infinitely better than the small, inadequate doses formerly given at intervals of one to six weeks. Insufficient doses at short intervals, as employed by the so-called "conservative" radiotherapeutists, simply encourages the tumor to become radioresistant, as was proved experimentally by Mottram.[3] Yet Martin [4] stated that as far back as 1913, Pusey [5] had devised a technic which gave a dose high enough to effect a cure but which, for some reason, was not then generally adopted.

There is no part of the body where cancer can be treated by radiation so satisfactorily as on the lip. This is because (1) the blood supply is good, giving a healthy tissue bed—a prerequisite for the establishment of radiosensitivity or a good effect from radium; (2) application is easy, and (3) metastasis does not take place until late in 90 per cent of the cases.

Classification.—Lain [6] reviewed the early period (1909 to 1921 inclusive) of the radiation treatment of cancer of the lip and concluded that on the whole the final results had been satisfactory. He stressed the importance of proper dosage and classified the lesions according to the extent of the clinical involvement. Other more recent classifications [7] have been based on measurements or on the duration and extent of the glandular involvement. We are convinced that a description of clinical characteristics is of the utmost importance, even though a simpler classification may be necessary when one tabulates results.

PRECANCEROUS CONDITIONS

The various kinds of cancer of the lip all seem to originate in certain precancerous conditions such as leukoplakia, sun or "fever" blisters, senile keratoses, keratoses due to irritation from jagged or broken teeth and granulomas arising in razor cuts or from simple scratches.

Leukoplakia.—The lips of many pipe and cigaret smokers show a thin type of leukoplakia, both on the vermilion border and on the mucous surface. This is distributed over definite areas of the lip, usually near the place where pipe, cigar or cigaret is habitually held. At first these are but thin, bluish white spots which are soft and seem to fade into the surrounding labial surface. As the condition develops, the spots coalesce to form small plaques with well marginated borders. At the point receiving greatest stimulation—the "smoker's patch"—there is a gradual thickening into leukokeratosis, a slightly warty proliferation spreading at first laterally in all directions, perhaps remaining in this stage for some time but eventually forming an indurated border with a rolled edge and a downgrowth beneath the leukokeratotic surfaces. Such lesions do not ulcerate or metastasize early but may suddenly begin to grow rapidly with a deep proliferation.

Actinic Lesions (Sun or "Fever" Blisters, Actinic Keratoses).—These were by far the most numerous early precanceroses noticed in our series. The patient's description of the earliest lesions is a blistering or sunburn in several areas on the vermilion border of the lower lip. Some had chronic actinic cheilitis of the entire exposed surface of the lip, with dryness, scaling and fissuring. With continued exposure to the sun a more persistent lesion is formed in one area. On examination this is seen to be an erosion, not a herpetic condition. There is usually some degree of superficial crusting; hence the term "fever" blister as used by the patients. These lesions heal but recur with exposure to the sun, after which two types of lesion seem to follow. The first is the formation over the blistered area of a keratotic scale which when peeled off yields a bleeding surface (keratosis solaris). Later a superficial induration spreads under this keratoma and infiltrates into the substance of the lip until a button-shaped induration can be palpated beneath the epithelium. The second type of lesion is one that sometimes develops rather rapidly from the sun erosion. After several recurrences, according to the patients, the erosion fails to heal and progresses into a denuded, slightly elevated, crusted, indurated growth. As this proliferates the borders become slightly elevated and infiltrated. Secondary infection, which invariably takes

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Because of lack of space, this article has been abbreviated for publication in THE JOURNAL. The complete article appears in the authors' reprints.

Read before the Section on Dermatology and Syphilology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 4, 1941.

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6. Lain, E. S.: Treatment of Cancer of the Lip by Radiation, Arch. Dermat. & Syph. **6**: 434-447 (Oct.) 1922.

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place, may eventually cause the growth to become fungating. Metastasis sometimes has been noted when the lesion was less than 2 cm. in diameter. This type is also found among the younger, more active patients. A pathologic study is being made on such lesions, but no discussion can be made in this paper except to state that the pathologic process of an early sun blister is similar to that produced by mechanical or chemical burns.

Senile Keratoses.—These are a frequent precursor of cancer of the lip in the aged. Ewing [8] mentioned cancer arising from seborrheic keratoses on the lip. In none of our cases did the cancer originate in the greasy, somewhat verrucous, yellowish brown, loosely adherent lesion known as seborrheic keratosis. But the dry, scaly, senile keratosis which is firmly adherent to the lip and is gray or brownish yellow may develop into a slightly elevated, indurated, button-like lesion which may proliferate in all directions and project 2 or 3 mm. into the substance of the lip before any ulceration takes place. These lesions often become large papillary growths which rise above the surface of the lip and form layers of keratin almost comparable to a cutaneous horn. Lesions arising from senile keratoses in the aged patient may reach huge proportions without showing any evidence of metastasis.

Leukokeratotic Areas.—These may arise from trauma from jagged or broken teeth and seem to have a predilection for the buccal mucosa of the lip, where they grow rapidly, ulcerate and metastasize early.

Superficial Granulomas.—On the lip these are the result of scratches, razor cuts and other abrasions. They tend to remain not more than 1 or 2 mm. in thickness and proliferate peripherally on the surface. They soon form a thin, soft, granulomatous mass which bleeds easily and becomes ulcerated and secondarily infected; the infection may lead to extensive local suppuration. The lymph glands are usually palpable because of an inflammatory reaction to this infection.

MATERIAL

The patients studied are classified according to the size of the lesion and the extent of involvement of the lymph nodes. They were all seen in private practice, and discussion of any patients from the outpatient department of the university hospitals will be so identified. We have found our patients more easily classified in the following manner:

Group 1—lesion 1.5 cm. or less, glands not palpable.

Group 2—lesion 1.5 cm. or less, glands palpable.

Group 3—lesion larger than 1.5 cm., glands not palpable.

Group 4—lesion larger than 1.5 cm., glands palpable.

In our series, 177 of the patients were in group 1, 48 were in group 2, 46 were in group 3 and 47 were in group 4.

The lesions of many patients of groups 1 and 2 were indurated, smooth, button-like proliferations. Some had become ulcerated because of previous treatment with plaster. Many were slightly elevated, with warty or scaly keratotic surfaces, indurated bases and rolled borders.

In groups 3 and 4 the patients had larger, ulcerative, granulomatous growths. Several growths extended over one third of the surface of the lip, while one lesion involved one half and another fully two thirds of the surface.

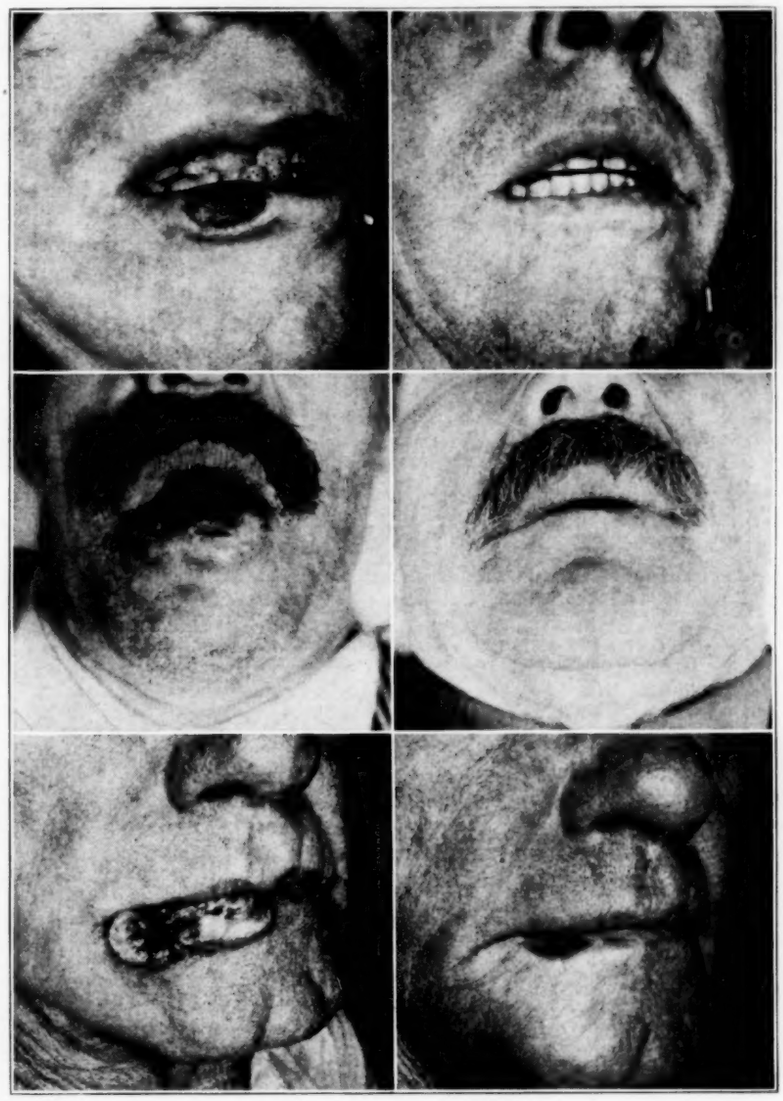

Fig. 1.—Three patients treated by well filtered radium and roentgen rays. *a*, patient in group 3 treated by interstitial needles and roentgen rays, with two year survival; *b*, patient in group 4 treated by external application of radium and roentgen rays, with five year survival; *c*, patient in group 4 treated by interstitial needles and roentgen rays, with four year survival.

Our patients were studied to determine the type of skin, the incidence of dental caries, the possible influence of their occupations, the kind of smoking (pipe, cigar or cigaret), the involvement of the lymph nodes and finally the evolution of the intensity of treatment with its subsequent results. The youngest patient treated was 20 years old and the oldest 85 (table 1). The average age was 53 years.

Age is a factor in selecting the type of treatment. Radiation sequelae as a contraindication to radiation therapy are negligible. Under less favorable circum-

8. Ewing, James: Neoplastic Diseases, ed. 4, Philadelphia & London, W. B. Saunders Company, 1940.

stances it is possible to obtain sequelae such as telangiectasia and slight atrophy. We have examined younger patients with tender skins who had been treated twenty years before by beta radiation and unfiltered

Fig. 2.—An early infiltrating lesion which shows disorganized, fairly anaplastic prickle cells breaking through the basal cell membrane. Intercellular edema with loss of prickle cells in some areas may be noted. One well formed epithelial pearl may be seen in the lower portion.

roentgen rays, and most of them still showed soft, pliable scars with excellent cosmetic results (only a few presenting small, telangiectatic areas), thereby demonstrating that the earlier technic produced many good results. Nowadays in younger patients (20 to 35 years old) we confine the treatment to gamma radiation, using interstitial needles or well filtered radium plaques.

PREDISPOSING CAUSES

Fair-skinned persons are particularly susceptible to cancer of the lip. Only 2 in our series were full-blooded Indians, and the growths occurred in the scars of old chronic lupus erythematosus. Only 4 women were found to have cancer of the lower lip. One hundred and four of our patients were farmers, showing again that occupation does play an important part. The chance of acquiring a malignant neoplasm of the lip is in proportion to the extent of exposure to actinic rays. The problem of actinic rays unfavorably affecting areas of radiodermatitis has been overcome largely in radiation treatment by improvements in technic, so that few serious consequences in this respect are now encountered. Sensitive patients must lead a less active life and so are advised to rest during the time of most intense exposure to the sun, to work only early and late in the day and to protect their lips with sunburn creams in which are incorporated bismuth oxylchloride, quinine or tannic acid. One of the agents now being tried for reflecting actinic rays is a proprietary preparation made in the form of a lipstick containing a skin-colored product. Patients with skin sensitive to actinic rays are advised to wear large hats and to use these creams or lipsticks several times a day. They are advised also to grow a heavy mustache, when possible, to protect the lips from the sun. Sixty patients in our study reported sun or "fever" blisters as initial lesions.

The use of tobacco predisposes to leukoplakia, which leads to leukokeratosis and finally to carcinoma. Sixty-three of our patients were cigaret smokers; 52 used a pipe, and 17, cigars. There were 132 smokers altogether. Thirteen patients reported previous abrasions with the razor, while many had dental caries or irregular or sharp teeth. Those having the worst oral conditions were advised to have oral hygiene and extraction of decayed teeth before high voltage roentgen therapy for metastasis was prescribed, in order to prevent necrosis of bone. Otherwise the mouth was not cleaned up until after the lip had been irradiated and was entirely well. Fifteen patients had been treated previously with pastes and plasters, therapy which, as Broders,[9] Lain [6] and others have agreed, lessens the chance of recovery. Eleven had been treated by fulguration (electric needle), 4 with acid, 1 with phenol and 1 with the silver nitrate stick. Six had received small repeated doses of roentgen rays in another clinic.

BIOPSY

There is general agreement among all who treat cancer that biopsy should be done whenever possible,

Fig. 3.—A highly undifferentiated tumor; solid cords of anaplastic squamous cells, with large vacuolated cells resulting from dyskeratosis, in some areas of a single cell type.

but it has not been our custom to take specimens for biopsy in all cases as a routine procedure. The largest number of lesions in patients of groups 1 and 2 showed

9. Broders, A. C.: Squamous Cell Epithelioma of the Lip, J. A. M. A. **74:** 656 (March 6) 1920.

no ulceration, and nonulcerated lesions were the type on which biopsy was not usually performed.

Since we began to use small interstitial needles biopsy has become a much simpler procedure and is performed more often, for in any event the lip must have local anesthesia for the placement of the needles, and a specimen for biopsy can be removed at the same time.

TABLE 1.—*Age of Patients*

Age	No.
20-30	15
30-40	56
40-45	30
45-50	39
50-55	30
55-60	34
60-65	39
65-70	30
70-75	24
75-80	15
Over 80	6
Total	318

GRADING

The importance of grading tumors according to Broders' classification of adult and embryonal cells is accepted with skepticism by many pathologists, but this method of classification has been a valuable contribution to the study of the pathology of tumors. In his excellent review [9] of the pathology of cancer of the lip, 62 per cent of the tumors were of grade 2 and 21 per cent were of grade 3.

Mekie [10] expressed the belief that the idea of differentiation of tumors is not the whole story. If the histogenesis of tumors is to be understood, the relationship of the squamous cells to the basal cells must be understood. He considered the basal cells as the important ones, since they alone possess the power of reproduction. The basal cell is the most highly differentiated in squamous epithelium, and the more superficial layers (stratum lucidum and stratum corneum) represent a "degeneration" which culminates in keratinization. He expressed the opinion that the tumor bed and the anaplasia of the basal cells in squamous cell carcinoma are of utmost importance.

Grading is considered to be of prognostic value. Broders found metastasis in 11 per cent of patients with tumors of grade 1 and grade 2, while 66 per cent with tumors of grade 3 or grade 4 had metastasis. But examination of 20 patients with metastasis by Kennedy [11] showed 18 with grade 1 and 2 with grade 2 cancers. Thus, in this small group it did not seem that grading played an important part in determining the danger of metastasis.

There are many other factors of equal prognostic value of a clinical nature. The type of tumor bed (MacKee and Cipollaro [12]) is of as great importance to the radiotherapeutist as the percentage of cells which are adult or embryonal. The gross appearance and clinical course of the tumor also are of much prognostic value.

TISSUE STUDIED

Seventy-one microscopic sections from lesions of the lower lip were studied. Forty-one were from private patients and 30 from outpatients (University Hospitals). Biopsy was done on only a small percentage of the 225 patients in groups 1 and 2. Of the 93 in groups 3 and 4 less than 50 per cent had sections made.

MODES OF USING RADIUM

1. *Application of Radium to the Surface.*—For the application of "cross fire" therapy, no part of the body is more satisfactory than the lip. Radium plaques are used in two forms approximately fitting the lesions. For larger growths, two 10 mg. half strength plaques and one 5 mg. plaque are used in the form of a saddle, the two 10 mg. plaques being placed anteriorly and posteriorly with the 5 mg. applicator on top. Two mm. of lead is used as a filter on all plaques, only the harder gamma rays thus being utilized. An additional distance of 1 to 1.5 cm. from the skin to the plaque is supplied by enclosing gauze between the filter and the nonmetalic rubber. It is left in place a long enough time to give the predetermined dose of 1,400 to 2,500 milligram hours, which is usually three or four days. During use of the saddle applicator, particular attention to the natural fulness and thickness of the lip is important, as the dose varies in proportion to the diameter of the lip.

2. *Use of the Interstitial Needle.*—Our needles vary in size, having an over-all length of 11, 21 or 28 mm. and a wall thickness of 0.5 mm. of platinum. The radium element is distributed so that there is 1 mg. to each centimeter of active length. This is slightly more radium element than there was in the original needles used by Cade,[13] but this distribution was used since it was found that the radium in a 1 cm. needle centrally placed for seven days would satisfactorily destroy 1 cc. of squamous cell carcinoma. In accordance with the previous work of other radiotherapeutists,[14] we have employed the following plan of irradiation: The entire tumor is divided into imaginary spheres of 1 cc. each. If the lesion is sufficiently wide, needles are placed in parallel rows, 1 cm. apart, running the length of the lesion. A second or a third plane of needles 1 cm. inferior to the plane first implanted is used if necessitated by the depth of the lesion. Thus at least 168 milligram hours of radium can be administered to each sphere or cubic centimeter of tissue. In order not to undertreat the peripheral cells of a tumor, the outer needles are placed 0.5 cm. beyond the border of the lesion in apparently normal skin.

TABLE 2.—*Duration of Illness*

Duration	No.
1 to 6 months	83
6 months to 1 year	55
1 to 1½ years	32
1½ to 2 years	13
2 to 3 years	29
3 to 4 years	10
4 to 5 years	12
5 to 6 years	8
Over 6 years	10
Total	252

Interstitial needles are of particular value in the treatment of recurrences of lesions previously inadequately treated by roentgen rays or by too small external applications of radium. Serious cutaneous reactions

10. Mekie, D. E. C.: Buccal Carcinoma, Am. J. Cancer **16**: 971-1023 (Sept.) 1932.
11. Kennedy, R. H.: Epithelioma of the Lip, with Particular Reference to Lymph Node Metastases, Ann. Surg. **99**: 81-93 (Jan.) 1934.
12. MacKee, G. M., and Cipollaro, A. C.: Cutaneous Cancer and Precancer, New York, American Journal of Cancer, 1937.
13. Cade, Stanford: Radium Treatment of Cancer, London, J. & A. Churchill, 1929.
14. Shelmire, J. B., and Fox, E. C.: Small Radium Needles in the Treatment of Malignant Cutaneous Tumors, Arch. Dermat. & Syph. **34**: 862-872 (Nov.) 1936. Martin, C. L.: Small Radium Needles versus Radon Implants, Am. J. Roentgenol. **27**: 240-248 (Feb.) 1932.

have been avoided by implanting the needles as deeply as possible while yet approximating the lower border of the lesions. Such placement allows the major effect of radiation to be utilized at a proper depth, whereas the amount of radiation affecting the skin will be small proportionately. We get better cosmetic results

TABLE 3.—*Site of Cancer*

Site	No.
Left side of lower lip	154
Center of lower lip	66
Right side of lower lip	93
Total	313

TABLE 4.—*Previous Treatment*

Type of Treatment	No.
Plaster	15
Electric needle	11
Acid	4
Phenol	1
Silver nitrate	1
Roentgen rays elsewhere	6
Total	38

in utilizing the same principle by interstitial irradiation, avoiding telangiectasia, pigmentary changes and atrophy. The gamma rays from this small concentration of radium over a more prolonged time seem to fulfil Regaud's [15] concept of bombarding the cells during the stage of mitosis. Interstitial irradiation has been used in our series for six years. Fifty-two patients were treated by this method, and for only 1 was failure to cure the primary lesion recorded. This patient had been treated previously several times by external application of small, inadequate doses of radium. Interstitial irradiation does not require hospitalization, though the area under treatment is dressed daily with a bland ointment. If the lesion is secondarily infected, filtered roentgen ray treatment is given for several days preceding the placement of the needles, and moist dressings of boric acid or sulfanilamide and glycerin are used.

In our series there have been no cases of lymphangitis or local suppuration in the lip resulting from the interstitial implantation of radium. Patients have but little discomfort, and the procedure saves valuable time formerly lost each day in removing the surface applicator for shaving and eating.

TREATMENT OF GROUP 1

Group 1 consisted of patients whose lesions were localized, indurated and not more than 1.5 cm. in diameter. 1. If the lesion is a papillary outgrowth, superficial in type, 1 cm. or less in diameter and not over 1 to 3 mm. in thickness, unfiltered roentgen rays are used, with a force of 100 kilovolts and an intensity of 3 milliamperes, in 3 to 5 skin erythema doses (800 to 1,200 r). The surrounding normal tissue is shielded within 2 to 3 mm. of the growth. In addition, surface applications of gamma radiation by means of needles or plaques are made, with a 10 mg. half strength plaque with 2 mm. of lead screening, or its equivalent, at a distance of 1 cm. for 480 milligram hours.

2. If the lesion is of the deeper, more infiltrative type, 15 mm. in diameter and 3 to 6 mm. thick, the roentgen rays are filtered through 1 to 2 mm. of aluminum, in doses of 800 to 1,000 r, in divided doses of 300 r every other day. In addition, two small 0.6 or 1.5 mg. interstitial needles are placed parallel to each other, 1 cm. apart, on each side of the lesion, for a total of one hundred and sixty-eight hours.

TREATMENT OF GROUP 2

The primary lesions in patients of this group are treated in much the same manner as the more infiltrated type in group 1. Palpable glands are not irradiated at the same time unless the nodes are large, hard, firm and clinically metastatic.

TREATMENT OF GROUPS 3 AND 4

In patients of groups 3 and 4 lesions from 1.5 to 3 cm. in extent are treated with interstitial needles and filtered roentgen rays in much the same manner as in groups 1 and 2. Growths larger than 3 cm., if fungating in type and infected, receive preliminary irradiation with filtered roentgen rays, 400 to 600 r daily, the factors employed being those previously mentioned, on successive days for four or five days before the implantation of the needles. The results of treatment of these larger lesions have been highly successful. Because there is a broader area treated by radiation, some degree of telangiectasia and scarring is noticeable in patients with thin, fair skin. However, the reaction induced by this method does not cause such atrophy as follows unfiltered beta radiation used in repeated doses (such as dryness, telangiectasia and ulceration). Even though such sequelae are in evidence, the lips are still moist and have a fairly normal texture, but protection from sunlight and abstinence from smoking should be maintained rigidly.

PALPABLE NODES

The total number of patients with palpable nodes was much smaller than the number of those whose nodes were not palpable (table 9), being 48 for group 2 and 47 for group 4. Eight in whom metastatic lesions developed were not originally in group 2 or group 4. Many times when the lesions are infected on the surface swelling of the nodes is merely an inflammatory response to a long-standing infection. In the treatment of such lesions we do not feel that high voltage roentgen rays in small doses given routinely as a prophylactic

TABLE 5.—*Carcinogenic Factors in Previous History*

Factor	No.
Use of cigarets	63
Use of pipe	52
Use of cigars	17
Cut with razor	13
Total	145
"Fever" and sun blisters	53

TABLE 6.—*Year of Treatment*

Year	No.	Year	No.
1921	1	1931	14
1922	2	1932	20
1923	3	1933	22
1924	10	1934	10
1925	12	1935	11
1926	11	1936	24
1927	23	1937	24
1928	21	1938	26
1929	29	1939	20
1930	23	1940	12
Total			318

15. Regaud, C.: On Curietherapy of Epitheliomas of the Tongue and of Their Following Adenopathy, Brit. J. Radiol. **30**: 361-367 (Oct.) 1925.

measure are of any value, but for glands thought to be the site of metastasis a full, adequate dose is recommended.

Since the swelling of nodes often proves to be of inflammatory origin, the routine practice of giving high voltage roentgen rays to the gland-bearing areas of all patients with cancer of the lip certainly is not warranted, but patients must be selected by expert clinical judgment for the trying ordeal of heavy roentgen irradiation of the neck. No entirely satisfactory plan for dealing with metastases to the cervical nodes has yet been devised. It is felt that both surgical intervention and irradiation must be resorted to, the method that is most suitable being selected for each patient. In our series, only 27 were treated by protracted, well filtered roentgen rays to the areas of lymphatic drainage.

TABLE 7.—*Distribution of Survival Periods*

	No.		No.
5 year survivals in group 1..	105	Ten year survival or more..	83
5 year survivals in group 2..	17	Five year survival or more..	73
5 year survivals in group 3..	19		
5 year survivals in group 4..	15	Total	156
Total	156		
1 to 5 year survival *			71
1 to 5 year survival †			25
Lip well when last seen, but patient was lost track of before 1 year			30
Lip well, but patient died from causes other than cancer.....			14
Total			296

* We are still in contact with the patients.
† We have lost contact with the patients.

BLOCK DISSECTION

We feel that block dissection should not be recommended in every case of cancer of the lip but should be recommended only in selected cases. It is contraindicated, according to Duffy,[16] if the primary lesion is uncontrolled, if the capsule of the node is infiltrated by carcinoma, if cross or bilateral cervical metastases are present, if distant metastases can be demonstrated or if the patient is in poor general condition.

One patient with a four year cure in our series had block dissection of a large solitary node and is now in fine general condition. Edwards [17] has had encouraging results from combining radon implants in the nodes with high voltage roentgen rays. Martin [4] has combined long needles containing a weak radium element with high voltage roentgen rays.

RESULTS OF TREATMENT

The results listed in tables 7, 8 and 9 show a high percentage of cures. This is largely because 70 per cent of the lesions seen in our clinic are 1.5 cm. or smaller in diameter, and our patients for radiation treatment are selected as carefully as those reported on by surgical groups. Patients with hopeless, advanced cancer with large, fungating growths involving the entire lip and those already showing large suppurative nodes are not given treatment with radium. If any radiation is given to such patients, it is only by heavily filtered roentgen rays, with 140 kilovolts and a filter of 6 mm. of aluminum or 170 to 200 kilovolts and copper and aluminum filters (patients so treated not included in this series). Two patients each with a single gland affected by metastasis were treated by block dissection; 1 had a four year cure; the other remains well after nine months.

REGRESSION OF THE PRIMARY LESION

We have not failed to cure the primary lesion in every case in which treatment has been with interstitial needles or there has been adequate radium therapy, as described, if the lesion has not been treated previously by inadequate doses of radiation. There was a total of 83 patients living and free from evidence of cancer for ten years or more and 73 for five years or more. The total treated to 1936 was 216, with 156 well at least five years, making the five year survival rate 72.2 per cent. A survey of 22 patients who died from cancer showed that more than 50 per cent were in group 4, 11 being smokers and 8 using a pipe. Two previously had been treated with escharotics (solution of potassium arsenite and nitric acid) and 1 with a hot cautery.

SYPHILIS

Association of syphilis with cancer of the lower lip has been small in our study, but results of irradiation have been equally good despite the syphilitic history. Treatment of the syphilitic infection was continued with smaller doses of arsenicals and larger amounts of the heavy metals.

COMMENT

The study of a series of 318 cases of cancer of the lip should permit drawing of certain profitable conclusions: The time we began radiation treatment falls into three definite periods in respect to the type of filtration and the amount of the dose: (1) an early period—1924 to 1932; (2) a middle period—1932 to 1935, and (3) a late period—1935 to 1941.

Early Period—1924 to 1932.—During this time we used unfiltered roentgen rays and inadequate aluminum and brass-filtered radium, thereby using mostly beta radiation. The dose was small and was repeated four or five times at intervals of six to eight weeks. The results of this treatment were satisfactory in many instances, but it was noted that doses were applied at six week intervals, sometimes over nine months' time, and that some lesions finally had to be destroyed by cautery or electrosurgical methods. The cosmetic results were excellent on the whole, but in patients who had repeated doses of unfiltered radiation, some telangiectasia and radiodermatitis resulted. The large lesions (in patients of groups 3 and 4) were seldom entirely cured by irradiation but had to be destroyed by other methods. A total of 158 patients (table 8) were treated in the early period, with 14 deaths due to the metastasis of cancer. Twenty-one had been well for at least a year when last seen or had died from other

TABLE 8.—*Comparison of Newer Technic with Older Technic with Regard to Five Year Survival Rate*

Result	Early Period (Inadequately Filtered Radiation) Number	Later Period (Well Filtered Radiation) Number
Death from cancer or incurable metastases	14	3
Death from other cause, patient well at least 1 year when last seen.....	21	4
2 to 3 year cure	18	..
5 year cure	105	51
Total	158	58
Percentage of 5 year cures.....	66.0	88.0
Total 5 year survival rate, 72.2%		

16. Duffy, J. J.: Conservative Procedure in Care of Cervical Lymph Nodes in Intraoral Carcinoma, Am. J. Roentgenol. **29**: 241-247 (Feb.) 1933.

17. Edwards, H. G. F.: Metastatic Cancer in Lymph Nodes of Neck, South. M. J. **32**: 905-911 (Sept.) 1939.

causes. Eighteen were in the groups with two to three year cures before they were lost track of. One hundred and five had survived for five years or more with no metastasis, contact with us being maintained during this period. The rate of five year cures for the early period was 66 per cent.

Middle Period—1932 to 1935.—This was an era in which more filtration was applied to the radium, with an increase in the length of time of treatment. One continuous well filtered application was found to be all that was necessary to produce a cure of the primary lesion. This technic, as previously described, employed the "housetop" or the "saddle" applicator in connection with roentgen therapy. The results were excellent, and the large lesions of patients in groups 2 and 4 were cured. Thus we entered into a period in which the primary lesion was almost 100 per cent curable by irradiation alone.

Late Period—1935 to 1941.—This was a continuation of the period in which the larger dose of well filtered radium was employed, but with more use of interstitial irradiation. Since the interstitial irradiation is distributed only to the labial lesion and 1 to 2 cm. of surrounding tissue, the tongue and other contiguous structures did not receive the pronounced secondary

TABLE 9.—*Classification According to Extent of Disease of Patients with at Least One Year Survival*

	Recovered		Lost Track of	Died from Cancer or Incurable Metastases		Total
	No.	Pct.		No.	Pct.	
Group 1						
Lesion 1.5 cm. or less, local.....	149	84	23	5	3	177
Group 2						
Lesion 1.5 cm., with nodes.....	43	89	3	2	5	48
Group 3						
Lesion larger than 1.5 cm., local..	39	87	3	4	9	46
Group 4						
Lesion larger than 1.5 cm., with nodes	35	74	1	11	24	47
Totals	266	83	30	22	7	318
Patients with no palpable nodes.....	188	84	26	9	4	223
Patients with palpable nodes.....	78	82	4	13	15	95
Totals	266	83	30	22	7	318

irradiation which was a drawback in the use of the "housetop" or the "saddle" applicator. In the two later periods a total of 160 patients were treated, with only 8 deaths definitely attributed to cancer at the time these statistics were compiled. Of 58 treated before 1936, 2 died from other causes before five years had elapsed, 2 were not located and 3 died of metastasis of the cancer. Fifty-one patients were living after five years, making the five year survival rate for the late period 88 per cent. One noteworthy observation has been made regarding the late period. There was a definite decrease in the size of the lesions, more of them being classified in group 1. This we feel has been due to two things: (1) the early decision to have the lesion removed, influenced by simplicity of radiation treatment without hospitalization, and (2) education concerning cancer among the laity and members of the medical profession, which has increased the chances of early diagnosis and made prompter treatment possible.

FOLLOW-UP STUDIES

The importance of a regular follow-up in cases of cancer of the lip cannot be stressed too much. All our patients are made to understand that the treatment includes observation every two months for a year and a half after the cure of the primary lesion, and after this period contact is maintained by correspondence. The patients are also requested to make a yearly visit during the rest of their lives.

CONCLUSION

1. Three hundred and eighteen patients with cancer of the lower lip were treated by roentgen rays and radium. Twenty-two have died or now have incurable metastases (7 per cent). There was a 72.2 per cent five year survival rate.

2. Protracted radium therapy with the element well filtered has produced a higher percentage of cures than did the older technic, which employed weaker doses at short intervals.

3. Results obtained by interstitial radiation therapy in a restricted number of patients surviving five years or more revealed 95 per cent evidence of cure of the primary lesion. In a much larger number of cases of less than five years' standing, there is every indication of an equally good outcome.

117 North Broadway.

ABSTRACT OF DISCUSSION

DR. JAMES R. DRIVER, Cleveland: This paper represents a large series of cases treated over a long period. The five year results in the period from 1932 to 1941 showed 88 per cent cures as compared to 65 per cent cures in the early period, when unfiltered radiation and infrequent treatments and other forms of therapy were given. This proves the superiority of modern technics of using radiation therapy. Hardly any two workers employ identical technics in giving radiation treatment. But the use of fractional roentgen ray doses according to the Coutard principle is used by the great majority of radiologists and dermatologists today. Its superiority over older methods of using roentgen rays has been unquestionably established. The authors' experience with interstitial irradiation by the use of low intensity heavily filtered radium needles showing 95 per cent five year cures is gratifying. My associates and I have been using this form of radium therapy for over ten years and in the treatment of cancer of the lip the results have been better than by any other form of treatment. It is especially indicated in the more extensive infiltrating type of lesion. The cosmetic results are excellent and late irradiation changes are less than when roentgen rays are used. We seldom use a combination of radium and roentgen rays in the treatment of lip cancer as used by the authors. The method perhaps has the advantage of being able to administer the total combined dose in a shorter period of time. A total dose of from 4,000 to 6,000 roentgens, depending on the character of the lesion, is of chief importance and it makes little difference whether it is given by the use of radium or by the use of roentgen rays as long as it is administered according to the principle of frequent divided doses of roentgen rays or by continuous interstitial irradiation over a period of a week to ten days by the low intensity radium needles. I agree with the authors that the question of voltage and filtration depends on the size and the degree of infiltration of the lesion. As was pointed out, cancer of the lip metastasizes comparatively late in the majority of cases. Nevertheless it is in these cases that the failures occur. We believe, as the authors do, that expert surgery and radiation are indicated in all operable cases.

DR. JOHN W. SPELLMAN, Brookline, Mass.: I wish to emphasize the treatment of the regional lymph nodes rather than the control of the local disease. It is clear that no matter how effectively the disease of the lip is destroyed it will be futile if the patient succumbs later to metastatic involvement of the glands of the neck. In 1939 Taylor and Nathanson analyzed 616 cases of cancer of the lip collected from three Massachusetts hospitals with a view to determining the best method of handling the problem of the treatment of the regional lymph nodes. The pathologist found microscopic disease in 20 per cent of the cases in which no lymph nodes could be felt before operation. This fact shows conclusively

that, if block dissection of the neck is not carried out as part of the original plan of treatment, the follow-up of this group should be careful and frequent during the first three years at least following whatever kind of local treatment is used. In the light of our present knowledge, it seems that certain general rules may be formulated to guide us in advising the safest procedure in the matter of the treatment of the cervical lymph nodes: 1. Prophylactic irradiation of the neck is never warranted, since if the glands are not involved intensive irradiation is unnecessary and even harmful, while if the glands are involved we do not believe that at present it is possible to "cure" cancer in lymph nodes by high voltage roentgen therapy. Irradiation of the neck is of course a useful palliative treatment when inoperable metastatic disease is present. 2. Routine prophylactic neck dissection is not necessary or advisable in cases in which there is a small primary lesion of low malignancy and with small or impalpable lymph nodes. A close follow-up should be maintained, however, for at least three years, because a definite, if small, percentage of this group will develop cervical node involvement. If delayed neck dissection is carried out promptly after suspicion of metastasis is present, cures can still be obtained in approximately 60 per cent of these cases. 3. In cases of cancer of the lip in which regional lymph nodes measuring over 1 cm. are present after the wound has healed or the irradiation reaction has subsided, the usual suprahyoid block dissection should be carried out on the side of the lesion or on both sides if the cancer is close to the midline of the lip. In a series of neck dissections in which the nodes measured 1 cm. or more, actual involvement was found in over 60 per cent.

DR. H. J. TEMPLETON, Oakland, Calif.: There always has been argument between the dermatologist, the surgeon and the radiologist as to the best treatment of cancer of the lip, and I think that it can be partially settled by saying that a certain treatment is best in the hands of that particular individual who is most familiar with it. I have favored the use of destructive methods of treatment such as surgical excision, electrocoagulation, electrosurgery or the use of the actual cautery over radiation, although I use radiation a great deal. In 1939 I began an analysis of the cases seen in my private practice over exactly the same period as those of Drs. Lamb and Eastland, 1925 to 1939. I did not include cases seen in clinic practice. My partners and I saw a total of 113 patients with epithelioma of the lower lip. Of these 110 were men and 3 were women. Our policy in regard to biopsies has been to omit them if the lesion is typically epitheliomatous in appearance. All of our patients were seen by three dermatologists and if there was any disagreement as to the clinical diagnosis a biopsy was done; but of 52 biopsies from 102 patients 49 showed squamous cell epithelioma and 3 basal cell epithelioma. Of the 113 patients, 102 were treated by us. Earlier in our experience we treated our patients by means of extensive electrocoagulation or electrodesiccation and followed this with from 3,000 to 5,000 roentgens of unfiltered roentgen x-rays. More recently we have been inclined to omit the irradiation as we have found that our results are just as good without it. Ten of the patients whom we treated were lost track of or died from other causes and are not included in our statistics. Of the 92 whom we could follow, 88 are classified as cured for periods varying from two to five years. One patient had a recurrence after our treatment with radium but electrodesiccation was then done and the patient was known to be well three years later. One patient who had a recurrence was treated elsewhere and recovered. One patient who had a recurrence was lost track of and hence the case has to be regarded as a failure. One patient died. Out of a total of 92 patients we have 89 who are known to have recovered and remained well from two to five years. I feel that the differential diagnosis and treatment of these purely ectodermal lesions belongs particularly in the field of dermatology.

DR. JOHN H. LAMB, Oklahoma City: Dr. Driver's technic somewhat parallels ours except that he uses radium alone with equally good results. Dr. Spellman has given an excellent review of the more conservative ideas of the surgical treatment, particularly with reference to routine block dissections in lip cancer. We have attempted in this review to show our end results of several years' experience in the treatment of lip cancer. There is no desire on our part to discredit other methods of treatment. In fact, we did not use radiation always alone; sometimes we use electrocoagulation and desiccation if it fails. I think Dr. Templeton's results are excellent. We feel that cancer of the lower lip is not the great problem, as it has been thought by many with the routine block sections and routine high voltage roentgen therapy to the gland bearing areas but we feel it is a disease that is amenable to certain simple forms of treatment in as high as 90 per cent of the cases.

Clinical Notes, Suggestions and New Instruments

DEVELOPMENT OF ACUTE EXFOLIATIVE DERMATITIS DURING ADMINISTRATION OF SULFATHIAZOLE

MARY WEINSTEIN, M.D., AND ALBERT H. DOMM, M.D.
PHILADELPHIA

The cutaneous manifestations of sulfathiazole intoxication have been recently described by Volini, Levitt and O'Neil.[1] They reported an incidence of 3.9 per cent in a group of 180 cases. Urticarial, erythematous, macular, papular, nodular and purpuric eruptions were encountered; the nodular lesion probably represented the advanced stage of a toxic rash and has been the most serious lesion, having been associated with a fatal outcome in a high percentage of cases.

Among 400 pneumonia patients treated with sulfathiazole reported from the Philadelphia General Hospital [2] the incidence of cutaneous rashes was 3.7 per cent. There were no cases of acute exfoliative dermatitis observed and to our knowledge there are no reports in the literature of this condition. It seems worth while that the following case be reported.

REPORT OF CASE

History.—R. A., a Negro aged 38, admitted March 17, 1941 to the Philadelphia General Hospital in the medical service of Dr. Edward Torrance, complained of fever and pain in the chest. For two weeks prior to admission he had a mild infection of the upper respiratory tract with weakness and malaise. On the day of admission a sharp, shooting pain in the right lower part of the chest, shortness of breath and a nonproductive cough suddenly developed. His past history was important in that he had a severe cutaneous rash about twelve years before during treatment for "bad blood," and following this attack he received no more "shots in the arm." The patient was well developed and well nourished, moderately dyspneic and acutely ill. The temperature was 101 F., the pulse rate 110, the respiratory rate 25 and the blood pressure 136 mm. of mercury systolic and 96 mm. diastolic. There was evidence of early consolidation of the right lower lobe. This was confirmed by roentgen studies on March 18. No other significant physical changes were noted.

Laboratory Examination.—A blood count revealed red cells 5,250,000 and white cells 16,900 with polymorphonuclear neutrophils 78 per cent, lymphocytes 21 per cent and monocytes 1 per

Dr. Domm is David Riesman Fellow in Medicine.
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From the Committee for the Study of Pneumonia Control, Philadelphia General Hospital.
Dr. Fred D. Weidman gave the description and made the interpretation of the pathologic changes in the skin. Dr. Harrison F. Flippin helped the author in the preparation of this report.

1. Volini, I. F.; Levitt, R. O., and O'Neil, H. B.: Cutaneous and Conjunctival Manifestations of Sulfathiazole Intoxication, J. A. M. A. **116:** 938 (March 8) 1941.

2. Flippin, H. F.; Reinhold, J. G., and Schwartz, Leon: Sulfapyridine and Sulfathiazole Therapy in Pneumococcic Pneumonia, J. A. M. A. **116:** 683 (Feb. 22) 1941. Schwartz, Leon, and Flippin, H. F.: Sulfathiazole in the Treatment of Pneumonia, Pennsylvania M. J. **44:** 446 (Jan.) 1941. Flippin, H. F.; Rose, S. B.; Schwartz, Leon, and Domm, A. H.: Sulfadiazine and Sulfathiazole in the Treatment of Pneumonia, Am. J. M. Sc. **201:** 585 (April) 1941.

cent. The Kahn precipitation reaction was negative. The blood urea nitrogen was 17 mg. per hundred cubic centimeters; blood sugar was 120 mg. A blood culture taken on admission was negative.

The urine had a specific gravity of 1.030; it was negative for albumin and for sugar and microscopic examination of the sediment was negative. Neufeld examination of the sputum failed to yield a type with antipneumococcic serum types I to XXXIII. Culture of the sputum contained pneumococci and Streptococcus viridans.

Course.—Between 10:30 a. m. March 19 and 6:30 a. m. March 21, the patient received a total of 15 Gm. of sulfathiazole [3] with equal amounts of sodium bicarbonate. On the morning of March 21 the temperature rose to 103 F.; the patient appeared more toxic and a diffuse macular rash was noted involving the neck, chest and arms. The diagnosis of drug rash was considered and treatment with sulfathiazole was ordered discontinued, although the patient did receive four

Eruption as it appeared twenty-four hours after onset. Courtesy of Dr. Leroy Latowskey.

additional 1 Gm. doses of the drug owing to an oversight in night orders. Within twenty-four hours the cutaneous lesions became vesicular, with exfoliation, and involved practically the entire surface of the body as shown in the illustration. There were no subjective symptoms except slight itching of the skin during the night.

The patient was seen on March 22 by Dr. Patricia Drant of the dermatology department, and a diagnosis of dermatitis medicamentosa due to sulfathiazole was considered most likely.

From March 21 to the time of his death on March 26, the patient's cutaneous lesions became progressively worse and were accompanied by a sustained fever of from 103 to 104 F. Examination of the blood on March 25 showed 3,500,000 red cells and 20,000 white cells with 68 per cent polymorphonuclear cells with a decided shift to the left, 28 per cent lymphocytes and 4 per cent monocytes Determination of sulfathiazole in the blood at this time showed no trace of the drug.

In addition to specific treatment with sulfathiazole, the patient received, before the cutaneous lesions developed, phenobarbital 1½ grain (0.1 Gm.) on three occasions, codeine sulfate ½ grain (0.03 Gm.) for four doses, morphine sulfate ¼ grain (0.015 Gm.) by hypodermic injection twice and six doses of elixir of terpin hydrate 1 fluidrachm (4 cc.). An ointment containing zinc oxide and boric acid was applied locally to the skin after the rash appeared.

Autopsy.[4]—At autopsy almost the entire cutaneous surface of the body was affected with the exception of the hands, forearms, feet and legs. Practically the entire back was denuded. The epiderm was exfoliated, leaving a brilliant red, shiny surface. This occurred in great patches, more or less extensive islands of persisting epiderm being interspersed. Nikolsky's sign was present on regions of involvement but not on the forearm, hands, feet and legs. There were no definite blebs; it appeared that the epiderm had simply been loosened from the corium.

On microscopic section the skin presented four important pathologic changes: First, there was a cleancut separation of the epiderm, unaccompanied by any frank inflammatory reaction. Reasonably, the exfoliation was a result of an accumulation of edematous fluid at the region of the basement membrane. The adjoining epidermal cells exhibited but a minor grade of edema, and it was not extreme in the corium immediately below. The epidermal cells in the prickle layer were by no means hyperplastic and the metabolism of melanin seemed to have been abrogated. Second, in connection with this edema, the basal cells had undergone a peculiar inflammatory metaplasia and hyperplasia. Third, the linings of the blood vessels showed definite hyperplasia and swelling of the lining endothelium. This, occurring uniformly and diffusely throughout the entire section, speaks for a hematogenous route for the etiologic agent. Fourth, the skeletal muscle fibers at the bottom of the section were swollen and had proliferative nuclei; the transverse striations had disappeared and the fibers were not completely hyalinized. This, likewise, speaks for a general constitutional factor, whether it is the antecedent pneumonia or the sulfathiazole.

The left lung weighed 510 Gm., the right lung 750 Gm. These organs were somewhat firmer than usual in the dependent portions but no areas of consolidation were found. When the tissue was compressed a small amount of yellow gray purulent material escaped from focal points on the cut surface. Microscopic section presented only emphysema, edema and chronic passive hyperemia. The heart was dilated and hypertrophied (weight 460 Gm.) and showed a mild degree of myocardial softening and coronary sclerosis. The kidneys, liver and spleen revealed no significant changes.

COMMENT

An acute exfoliative dermatitis developed in a patient suffering from an atypical pneumonia after receiving 15 Gm. sulfathiazole and he died. The abrupt onset of cutaneous involvement, increasing fever and progressive toxicity during sulfathiazole therapy for pneumonia together with the finding at postmortem of the unusual dermatologic process suggests that this case represents an instance of acute exfoliative dermatitis due to sulfathiazole. Other than an overwhelming toxemia resulting from the widespread and severe involvement of the skin, no satisfactory cause of death was found. Neither clinically nor microscopically did this dermatologic process resemble anything with which we are familiar except Ritter's disease. This, which is also known as dermatitis exfoliativa neonatorum, concerns infants exclusively and usually involves the face and there are not the degenerative changes in the capillaries which were exhibited in this case. It is of significance that this patient experienced a cutaneous rash in 1929 following intravenous therapy, presumably from arsphenamine, for "bad blood."

Certainly the potential danger of sulfathiazole dermatitis should be kept in mind with the first appearance of cutaneous lesions. Withdrawal of the drug and forcing of fluids at the earliest sign of cutaneous manifestations constitute the safest procedures, although, as demonstrated in this case, the outcome may still be fatal.

3. The sulfathiazole used in this hospital was free of phenobarbital contamination.

4. The autopsy was performed by Dr. Earl Keller.

COLLAPSE FOLLOWING PARENTERAL ADMINISTRATION OF SOLUTION OF THIAMINE HYDROCHLORIDE

LEON SCHIFF, M.D., CINCINNATI

The following experience is being reported because, as far as I am aware, a similar case has not been recorded and because it deals with a therapeutic substance which is frequently used at present.

A school teacher aged 45 had been suffering with a mild form of Raynaud's disease since 1932 and with a progressive hypertrophic arthritis of the lumbar spine and sacro-iliac regions since 1933. In April 1940 she had a severe attack of right-sided sciatica for which, among other measures, injections of thiamine hydrochloride were started. A total of thirty-six intramuscular injections of 25 mg. was given between April 16 and July 10, with two different commercial preparations. She vomited twenty minutes and one hour after her eighteenth injection on May 21, 1940.

No more thiamine hydrochloride was given until August 6, at which time the first preparation used was resumed. By August 16 she had received six injections with either nausea or vomiting following four of them. Administration of a third preparation was begun August 24 and continued to September 7, for a total of five injections. This preparation was resumed October 7, and ten injections were given up to December 20.

On December 28, about one or two minutes after receiving her injection of thiamine hydrochloride into the buttocks (from a 5 cc. vial from which she had had six previous injections), the patient became nauseated and vomited. A thin, colorless fluid issued from her nose; she voided involuntarily and collapsed. Her skin was covered with a cold perspiration. She was pulseless and had ceased breathing, and her heart sounds were inaudible. She was placed on a table in shock position and surrounded with covers. Artificial respiration was started, and 1 cc. of solution of epinephrine hydrochloride was injected intravenously. She was also given 1 cc. of epinephrine subcutaneously and 7½ grains (0.5 Gm.) of caffeine with sodium benzoate intramuscularly. Her blood pressure could not be obtained at first. About half an hour later her pulse was palpable and her blood pressure was 110 systolic and 70 diastolic. On being questioned following her recovery, she stated that she had had short bouts of sneezing a short time after the last three or four injections of the thiamine hydrochloride.

On Jan. 2, 1941, an intradermal scratch test done with two of the commercial preparations resulted in a definite white wheal surrounded by an area of hyperemia which itched and reached its maximum in from fifteen to twenty minutes, at which time slight nausea and coughing occurred. On January 25, scratch tests done with 0.5 per cent solution of chlorobutanol, used as a preservative in the first preparation, and with a solution of hydroxyquinoline sulfate, which was used as a preservative in the last preparation, were negative. A similar test done with an aqueous solution of thiamine hydrochloride was positive. There was a white wheal 1 cm. in diameter surrounded by an area of erythema about 3 cm. in diameter, reaching a maximum size in twenty minutes. The intradermal test repeated on February 1 with an aqueous solution of thiamine hydrochloride was again positive. A passive transfer test performed by Dr. Albert Zoss on February 27 was negative.

This experience strongly suggests that the shock suffered by the patient may have been due to sensitivity to solution of thiamine hydrochloride. In view of the rapidity with which the reaction occurred, it is assumed that some of the thiamine hydrochloride must have been administered intravenously on the occasion of the last injection.

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Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

ACTIVATED STEROLS IN THE TREATMENT OF PARATHYROID INSUFFICIENCY

A REVIEW

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This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of Glandular Physiology and Therapy. The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—ED.

It is now well established that certain products derived from activated ergosterol are highly effective in increasing the concentration of calcium in the blood and in relieving the symptoms of parathyroid insufficiency. It appears, from some years of accumulated clinical experience, that these products may be administered over a considerable time with reasonable safety, provided proper precautions are observed, and that their prolonged use is attended neither by injury to the patient nor by the development of tolerance.

The subject of the management of hypoparathyroidism with the activated sterols assumes especial importance because of the fact that substitution therapy, in the form of administration of solution of parathyroid, is virtually limited to rather acute conditions, in which the treatment needs to be continued for days or weeks rather than months.[1] Not only is no tolerance to the activated sterols developed but they also have the decided advantage that the preferable method of administration is by mouth. On the other hand, the action of the sterols is somewhat delayed, so that for the relief of acute parathyroid tetany solution of parathyroid may be indispensable.

Reviews of the use and limitations of solution of parathyroid are available.[2] This review presents the principles underlying the use of the activated sterols in the treatment of parathyroid insufficiency, current knowledge concerning the mode of their action, a consideration of their toxicity and a brief summary of clinical experience with the preparations at present available for this purpose. Because of the unwarranted implication in the current literature that the beneficial effects of one of the derivatives of irradiated ergosterol (dihydrotachysterol) in hypoparathyroidism are specific for that substance, it will be necessary to emphasize the evidence to the contrary. The conclusion is reached that similar, if not identical, effects may be obtained from several of the activation products of ergosterol and cholesterol and that there is no satisfactory evidence that the therapeutic effects of dihydrotachysterol are superior to those of vitamin D when the latter is given in comparable doses. This review does not consider the use of vitamin D products for purposes other than to regulate the concentration of calcium in the plasma.

From the Department of Physiology, University of Chicago.

1. Aub, J. C.: Parathyroid Hormone Therapy, in Glandular Physiology and Therapy, Chicago, American Medical Association, 1935, pp. 379-385; J. A. M. A. **105**: 197-199 (July 20) 1935.
2. Shelling, D. H.: The Parathyroids in Health and in Disease, St. Louis, C. V. Mosby Co., 1935. Aub.[1]

CHEMISTRY AND PREPARATIONS

The distinction between the antirachitic action of the irradiation products of ergosterol and those actions which are responsible for the toxicity of certain of these products was first clearly drawn by Holtz and Schreiber [3] in 1930. They were unable to make a preparation which was antirachitic but nontoxic but by appropriate chemical treatment could destroy most of the antirachitic action while retaining and actually increasing the toxic effects. As a reference to the dominating symptoms of the toxic actions of irradiated ergosterol—hypercalcemia and pathologic calcification in the soft tissues—they named the principle responsible for these effects the calcinosefaktor. Holtz and his co-workers were then responsible for the further study of this factor, here called the "calcemic principle," and eventually [4] for its introduction into clinical use in the form of dihydrotachysterol, originally known and frequently referred to in the literature as A. T. 10 (antitetanic preparation 10).

TABLE 1.—*Vitamin D Activity and Toxic Borderline Doses of Various Derivatives of Irradiated Sterols*

	Vitamin D Activity, I. U. per Mg.	Toxic Borderline Dose,* Mg.
Calciferol	40,000	0.05-0.07-0.125 (Morris and McLean.[37] Holtz, Gürsching and Kraut.[40] Shohl and Farber [44])
Dihydrotachysterol		
Crystalline, pure	200 [5]	0.010 [5]
Commercial, A. T. 10	80-100 (Harnapp, G. O.: Monatschr. f. Kinderh. **63**: 262, 1935. Shohl and Farber [44])	0.025 [9]
Toxisterol	Little or no antirachitic activity	0.025 [40]
Tachysterol	Little or no antirachitic activity	0.200 [40]
Lumisterol	Little or no antirachitic activity	Not toxic

* All the data on toxic borderline doses are obtained from observations on mice, by the method described,[10] except for the observations of Morris and McLean [37] and of Shohl and Farber,[44] which were obtained on rats by comparison with dihydrotachysterol.

The action of the calcemic principle is nonspecific [5] and is shared by vitamin D_2, vitamin D_3, 22-dihydrovitamin D_2, dihydrovitamin D_2 II, tachysterol, dihydrotachysterol, 22-dihydrotachysterol and probably also toxisterol. Of these, only vitamin D_2, in the forms of crystalline calciferol and of viosterol, and dihydrotachysterol have received sufficient investigation and clinical trial to warrant a review of their usefulness in the treatment of hypoparathyroidism. Toxisterol appears to have toxic actions qualitatively different from those of the other substances considered.[6]

The chemistry of the activated sterols has been reviewed by Bills.[7] Irradiation of ergosterol leads to the following chain of reactions: ergosterol→lumisterol →tachysterol→calciferol (vitamin D_2). Further irradiation leads to formation of toxisterol and of the suprasterols I and II. More radiant energy is required to decompose calciferol than to produce it, so that when irradiation is not unduly prolonged calciferol is the chief product.

Calciferol is vitamin D_2 and is available in pure crystalline form. The international unit (I. U.) of vitamin D, which is quantitatively the same as the U. S. P. unit, is equivalent to 0.000,025 mg., or 0.025 micrograms of crystalline calciferol. One milligram of calciferol is equivalent to 40,000 international or U. S. P. units of vitamin D. Vitamin D_3 is activated 7-dehydrocholesterol and is the chief form in which vitamin D is present in fish liver oils.

Viosterol is the nonproprietary name adopted by the Council on Pharmacy and Chemistry of the American Medical Association [8] for all acceptable preparations of irradiated ergosterol. Under the best conditions of preparation it is composed of approximately 50 per cent of calciferol, with lumisterol and tachysterol accounting for most of the remainder.[7] It is standardized in terms of its vitamin D activity, so that the content of lumisterol and tachysterol, which have little or no antirachitic effect, are not taken into account. In ordinary use, for the prevention or treatment of rickets, the amounts of these substances administered are negligible, but when doses sufficient to produce the calcemic effect of vitamin D are given tachysterol will contribute appreciably to this effect. Lumisterol has not been shown to have any toxic, or calcemic, effect.

The chemistry of dihydrotachysterol, including the method of preparation of a pure crystalline product, has been described in detail by von Werder.[5] Dihydrotachysterol differs from calciferol only in the saturation of a double bond, but this difference is sufficient for the disappearance of all but a small fraction of the antitrachitic action and for a decided enhancement of toxicity. Dihydrotachysterol is formed when tachysterol, one of the irradiation products of ergosterol, is treated with sodium and propyl alcohol. It is available only in the form of an oily solution, described as containing 5 mg. of the basic substance per cubic centimeter, of which approximately 2 mg. is pure dihydrotachysterol.[5]

Holtz and his co-workers [10] introduced a biologic method by which the available preparation of dihydrotachysterol is standardized. A "toxic borderline dose" is the amount which when given in ten single daily doses over a period of thirteen days to a series of 8 male mice weighing from 16 to 18 Gm. will produce a loss in weight of more than 2.5 Gm. or death in at least 50 per cent of the animals.[9] Table 1 summarizes the available information concerning antirachitic activity and toxicity of the preparations considered in this review.

DOSAGE AND TOXICITY

It will be shown that much confusion over the use of vitamin D in the management of hypoparathyroidism has arisen from the fact that there are two distinct dosage ranges for this substance. The prophylactic and curative range for the antirachitic effect, with which this review is not concerned, is ordinarily 700 to 1,000 international units a day.[11] The dosage necessary for the elevation of a subnormal serum calcium and its maintenance at a normal level is commonly 60,000 to 200,000 international units daily and may be even

3. Holtz, F., and Schreiber, E.: Einige weitere physiologische Erfahrungen über das bestrahlte Ergosterin und seine Umwandlungsprodukte, Ztschr. f. physiol. Chem. **191**: 1-22, 1930.
4. Holtz, F.: Die Behandlung der postoperativen Tetanie, Arch. f. klin. Chir. **177**: 32, 1933.
5. von Werder, F.: Ueber Dihydro-tachysterin, Ztschr. f. physiol. Chem. **260**: 119-134, 1939.
6. Shohl, A. T.: Personal communication to the author.
7. Bills, C. E.: The Chemistry of Vitamin D, in the Vitamins, Chicago, American Medical Association, 1939, pp. 443-458; J. A. M. A. **110**: 2150-2155 (June 25) 1938.
8. New and Nonofficial Remedies, Chicago, American Medical Association, 1940.
9. Footnote deleted on proof.
10. Holtz, F.; Laquer, F.; Kreitmair, H., and Moll, T.: Beiträge zur Kenntnis des Vitamins D.: I. Mitteilung: Die Wertbestimmung im Tierversuch, Biochem. Ztschr. **237**: 247-275, 1931.
11. Park, E. A.: The Therapy of Rickets, J. A. M. A. **115**: 370-379 (Aug. 3) 1940.

higher over short periods. Administration of dihydrotachysterol has been completely divorced from the system of units by which vitamin D preparations are standardized and, being standardized only in terms of its calcemic principle, is free from the confusion that exists in the case of vitamin D. Since the calcemic principle, common to both vitamin D and dihydrotachysterol, is identical with the factor responsible for the toxic manifestations of overdosage with both sterols, and since the desirable therapeutic effect depends on the administration of subtoxic doses of these substances, the question of dosage will here be considered in relation to toxicity.

The effectiveness of the calcemic principle is affected by the degree of parathyroid insufficiency, by the intake of calcium and phosphorus, by the female hormone, and perhaps by other physiologic variables. For this reason there are no absolute standards of dosages necessary to produce therapeutic or toxic effects. The available information, however, does not permit of any quantitative treatment of the subjects of dosage and toxicity in relation to the other variable factors concerned.

Initial Dosage.—Treatment of parathyroid insufficiency is commonly initiated with relatively large doses of the activated sterols, followed by smaller maintenance doses. Initial and maintenance doses will be considered separately.

Relatively large doses of dihydrotachysterol have been used and recommended for initiating treatment of acute attacks of hypoparathyroidism. More common practice, in chronic parathyroid insufficiency, is to initiate treatment with from 1 to 4 cc. daily of the oily solution (5 to 20 mg. of the basic substance). As it will be shown that at least 10 mg. of calciferol is required for a calcemic action equivalent to that of the 5 mg. of basic substance contained in 1 cc. of the solution of dihydrotachysterol, a corresponding daily dose of calciferol would be 10 to 40 mg., or 400,000 to 1,600,000 international units of vitamin D.

While these doses have the appearance of being enormous, owing to the system of units employed, there is little evidence of harmful effects of such doses, administered over relatively short periods. Spies and Hanzal [12] gave as much as 18,000,000 international units of vitamin D a day, in the form of viosterol, for from nine to twenty-five days to patients about to die of disease. They observed no symptoms referable to the medication, except for a rise in the serum calcium level to as high as 16.6 mg. per hundred cubic centimeters, and at autopsy found no pathologic calcification or other changes which they could attribute to the vitamin D. Steck and his associates [13] administered as much as 3,000,000 international units of vitamin D a day for fifteen days to a normal subject without evidence of disturbance of any kind. Single doses of vitamin D, commonly about 600,000 international units, are now frequently administered to infants in the so-called Stosstherapie of rickets, the literature having been reviewed by Vollmer [14] and by Reed, Struck and Steck.[15] Cowdry and Scott [16] reported giving viosterol to monkeys, of less than 3 Kg. body weight, in doses amounting to 27,600,000 international units of vitamin D within two hundred hours. They made no mention of clinical symptoms. Goormaghtigh and Handovsky [17] reported lethal effects on 4 dogs following single doses of 13 to 20 mg. (520,000-800,000 international units) of calciferol per kilogram of body weight. Five other dogs, given from 2.9 to 8 mg. per kilogram, survived.

Much of the earlier literature on the toxicity of vitamin D preparations must be discarded, owing to the wide use of a preparation of irradiated ergosterol with low vitamin D and high toxisterol content.[18] In the literature of the past few years I have been able to find no report of serious toxic effects from large initial doses of dihydrotachysterol and only one case following large doses of vitamin D over a relatively short period of time. A case is reported [19] of an obese physician aged 74 with generalized arteriosclerosis who took by mistake 2,300,000 international units of vitamin D, in the form of a concentrated solution of viosterol, daily for eighteen days, or a total of more than 40,000,000 international units. Nausea, anorexia, weakness, increased thirst and polyuria developed and finally he went into coma and died.

Maintenance Doses.—The dosage of the activated sterols necessary to maintain the serum calcium within normal limits, and to avoid the symptoms and sequelae of hypoparathyroidism, is dependent on the subject and certain physiologic variables, more particularly the degree of parathyroid deficiency present and the intake of calcium and phosphorus, and varies within wide limits. The extreme limits for dihydrotachysterol are given as from 0.15 to 1.0 cc. (0.75 to 5 mg. of the basic substance) daily. More commonly 0.3 to 0.5 cc. a day is needed. An equivalent dose of calciferol would be from 1.5 to 10 mg. (60,000-400,000 international units) a day for the extreme limits, and 3 to 5 mg. (120,000-200,000 international units) for the more commonly prescribed dose. The same variability, but within approximately the same limits, in the amounts of calciferol actually found to be necessary for maintenance doses is reviewed later.

Reports of accidental poisoning with vitamin D preparations, even when administered over long periods, have been rare in late years, most of the literature on the toxicity of these preparations having come from the deliberate administration of large doses in conditions other than hypoparathyroidism. In this connection Steck, Deutsch, Reed and Struck [18] have made an exhaustive investigation of the toxicity of vitamin D. For the most part they used concentrated preparations of viosterol, but comparable results were obtained with crystalline calciferol. They conclude that both human subjects and dogs generally survive administration of 20,000 international units of vitamin D per kilogram of body weight daily for indefinite periods without intoxication. Out of 773 human subjects receiving more than 100,000 international units daily over variable periods, 63 showed toxic symptoms, but with no deaths and with no effects from which recovery did not occur. Steinberg [20] administered a preparation of vitamin D, usually in doses of 160,000 international units a day, for periods of several weeks to one and one-half years,

12. Spies, T. D., and Hanzal, R. F.: Experimental Production of Hypercalcemia in Human Beings by Means of Irradiated Ergosterol, Proc. Soc. Exper. Biol. & Med. **31:** 747-750 (March) 1934.
13. Steck, I. E.; Deutsch, H.; Reed, C. I., and Struck, H. C.: Further Studies on Intoxication with Vitamin D, Ann. Int. Med. **10:** 951-964 (Jan.) 1937.
14. Vollmer, H.: Treatment of Rickets and Tetany by Parenteral Administration of One Massive Dose of Vitamin D, J. Pediat. **16:** 419-432 (April) 1940.
15. Reed, C. I.; Struck, H. C., and Steck, I. E.: Vitamin D, Chicago, University of Chicago Press, 1939.
16. Cowdry, E. V., and Scott, G. H.: Effect on Monkeys of Small Doses of a Concentrated Preparation of Viosterol, Arch. Path. **22:** 1-23 (July) 1936.
17. Goormaghtigh, Norbert, and Handovsky, Hans: Effect of Vitamin D_2 (Calciferol) on the Dog, Arch. Path. **26:** 1144-1182 (Dec.) 1938.
18. Bills, C. E.: Physiology of the Sterols, Including Vitamin D, Physiol. Rev. **15:** 1-97 (Jan.) 1935.
19. Kerr, W. J., in discussion of paper by Freyberg, Grant and Robb.[21] Steck, Deutsch, Reed and Struck.[13]
20. Steinberg, C. L.: Massive Doses of Vitamin D in Chronic Arthritis: Its Effect on Calcium Metabolism, J. Lab. & Clin. Med. **24:** 17-24 (Oct.) 1938.

to 40 patients and observed no untoward effects. He concludes that the "toxicity [of vitamin D] has been overemphasized." On the other hand, Vrtiak and Lang [21] administered from 150,000 to 250,000 international units a day to 20 patients and report that all became nauseated and in a few frequency of urination and nocturia developed. In one of Stacey's cases [22] the serum calcium rose to 15 mg. per hundred cubic centimeters after long administration of from 4 to 8 mg. (160,000-320,000 international units) of calciferol daily. In another of his cases 728 mg. of calciferol in five months, or an average of 4.8 mg. (192,000 international units) a day, led to loss of weight, anorexia and epigastric pains after meals. All the symptoms disappeared when the treatment was discontinued.

Ross and Williams [23] reported 4 cases of intoxication, with 2 deaths, in infants at the ages of 8 to 14 months, who received 20,000 to 40,000 international units of vitamin D a day in the form of a concentrated preparation of viosterol over a period of several months. An autopsy was performed on one patient and extensive metastatic calcification was found. In one of the patients who survived the serum calcium reached a level of 18 mg. per hundred cubic centimeters. Thatcher [24] reported a case in which a diagnosis of hypervitaminosis D was made at autopsy on a baby aged 11½ months from the finding of pathologic calcification in the kidney. The baby had never received more than about 600 international units of vitamin D in the form of cod liver oil a day and had usually received less. Other similar cases, reported as poisoning with vitamin D, were noted by Reed, Struck and Steck.[15]

No reports of fatal poisoning with dihydrotachysterol have been found. Rose and Sunderman [25] reported serious symptoms following 2 cc. a day for twenty-six days; on the other hand, Curtis [26] gave 3 cc. daily during the last four months of pregnancy, the latter dose being the equivalent, in calcemic action, of 30 mg. (1,200,000 international units) of calciferol a day.

Symptoms and Pathology of Intoxication.—I have emphasized in this review that the toxic actions of the activated sterols may be dissociated from the antirachitic action of these substances and that the "calcemic principle," which causes elevation of the serum calcium, is identical with the characteristics of the sterols responsible for their toxic actions. Consequently therapeutic use of the calcemic principle depends on the administration, usually over long periods, of subtoxic doses of certain of the activated sterols.

Reed [15] took a different point of view. He dissociated the toxic reactions from vitamin D from the hypercalcemia and based his belief that the two reactions are "distinct, or only incidentally related," on the observation that "hypercalcemia of extreme degree may occur without intoxication and that severe intoxication to the lethal stage may occur without hypercalcemia." He reported that in his laboratory 5 dogs had died, with unquestionable symptoms of intoxication, in which hypercalcemia was never observed, and I have had a similar experience. Moreover, it is a matter of common observation, both in dogs and in man, that there is no absolute correlation between the calcium level and the severity of other toxic manifestations in hypercalcemia.

From a theoretic standpoint these two points of view may perhaps be reconciled by recognition of the fact that hypercalcemia is one symptom of the toxic action and that its occurrence depends on a combination of circumstances, of which one is mobilization of calcium salts from the bones. Reed [27] demonstrated in balance experiments that increased excretion of calcium of pronounced degree may occur without hypercalcemia under the influence of large doses of vitamin D. It may be assumed that mobilization of the bone salt is a more or less constant manifestation of toxicity and that as a rule, but not invariably, this mobilization leads to an increase in the calcium level in the blood.

From the practical standpoint the question is not so much that of the identity or nonidentity of the toxic and calcemic principles of the activated sterols as it is whether elevation of the serum calcium, when desired, may be uniformly produced and maintained, without the occurrence of serious acute or chronic toxic manifestations. A few cases, refractory to dihydrotachysterol, have been reported.[28] The symptoms and pathologic manifestations of intoxication, as observed in man and in animals, will be discussed here.

According to Reed and his collaborators,[27] the earliest symptoms of intoxication, more commonly seen in man, resulting from administration of excessive doses of vitamin D preparations, are anorexia, frequency of urination and loss of weight in excess of that expected from the lessened food intake. If administration of the sterol is continued, gastrointestinal discomfort, vomiting, persistent nausea, muscular atony, headache, lassitude, polyuria and diarrhea, sometimes with bloody stools, may follow. In the fatal case with the fatal outcome reported by Kerr [19] similar symptoms were followed by coma and death, as they also are in animals.[13] In general, and if the dosage has not been excessive, the symptoms of intoxication disappear rapidly on cessation of administration of the toxic agent, but Freeman and Farmer have reported [29] and we have confirmed, the persistence of hypercalcemia and of other symptoms in dogs for as long as a month after the last dose of vitamin D. Moreover, as a rule, once toxic symptoms appear they are not relieved unless administration of the substance responsible is discontinued.[15]

The pathologic changes following intoxication with the activated sterols have been reviewed by Reed, Struck and Steck.[15] In addition to the changes in the bones, discussed in another section of this review, the important finding is calcification in the soft tissues. The kidney is most frequently involved, but the lungs and the thyroid are also found to contain areas of calcification in many instances. Calcification of the aorta also occurs in dogs following long-continued administration of subtoxic doses of vitamin D.

Goormaghtigh and Handovsky [17] have investigated the effects of calciferol on the dog, with special reference to the arterial system. They found that doses of about 0.1 mg. (4,000 international units) per kilogram a day are harmless, but doses of from 0.6 mg. (24,000 international units) per kilogram a day cause regressive

21. Vrtiak, E. G., and Lang, R. S.: Observations on the Treatment of Chronic Arthritis with Vitamin D, J. A. M. A. **106**: 1162-1163 (April 4) 1936; correction, ibid. **106**: 1828 (May 23) 1936.

22. Stacey, R. S.: Treatment of Low-Calcium Tetany with Calciferol, Lancet **2**: 656-658 (Sept. 21) 1935.

23. Ross, S. G., and Williams, W. E.: Vitamin D Intoxication in Infancy, Am. J. Dis. Child. **58**: 1142 (Nov.) 1939.

24. Thatcher, L.: Hypervitaminosis D, Lancet **1**: 20-22 (Jan. 4) 1936.

25. Rose, E., and Sunderman, F. W.: Effect of Dihydrotachysterol in Treatment of Parathyroid Deficiency, Arch. Int. Med. **64**: 217-227 (Aug.) 1939.

26. Curtis, J. K.: Parathyroid Insufficiency Treated with Dihydrotachysterol (A. T. 10), M. Clin. North America **24**: 833-840 (May) 1940.

27. Reed, C. I.: Personal communication to the author.

28. Holtz, F.: Nebenschildrüseninsuffizienz, Deutsche med. Wchnschr. **65**: 750-752 (May 12) 1939.

29. Freeman, S., and Farmer, C. J.: Correlated Studies of Calcium, Inorganic Phosphorus and Serum Phosphatase in Normal Animals and in Animals Influenced by Irradiated Ergosterol, Am. J. Physiol. **113**: 209-220 (Sept.) 1935.

lesions in arterioles, leading to cell necrosis in from seventeen to forty-five days. This is in close agreement with the toxic threshold of 20,000 international units per kilogram a day, established by Steck, Deutsch, Reed and Struck.[13] According to Goormaghtigh and Handovsky, the smooth muscle cell of the artery wall can recover as long as the necrotic stage has not been reached.

I have found little evidence in the literature of chronic injury in man resulting from administration of dihydrotachysterol or of products of vitamin D, but the possibility of such injury is by no means excluded. Reed, Struck and Steck[15] stated that their extensive use of vitamin D in large doses has not indicated that any chronic injury is to be expected if toxicity has not occurred, and that even when toxic effects have been observed it seems improbable that any residual chronic effects will follow. This is in agreement also with the recent report of Holtz[28] on the prolonged use of dihydrotachysterol.

MODE OF ACTION

The activated sterols, like the parathyroid hormone, owe their usefulness in the treatment of parathyroid insufficiency primarily to their ability to control the mobilization of calcium salts from the bones and thereby regulate the concentration of the calcium ion in the blood. The property of the sterols which is responsible for this action, and which has been designated the "calcemic principle," is regarded in this review as identical with the property which, in sufficiently large doses, leads to toxic symptoms, and in fact the hypercalcemia produced by the activated sterols in normal animals is itself a manifestation of the toxic action.

The ordinary antirachitic doses of vitamin D are generally believed to produce their effects by increasing the net absorption of calcium, and perhaps also of phosphates, from the gastrointestinal tract. While infants with low calcium tetany associated with rickets usually respond to antirachitic doses of vitamin D by a rise in serum calcium, the effect of such doses on the absorption of calcium is not sufficient of itself to produce a rise of the serum calcium level either in normal individuals or in individuals with hypocalcemia resulting from parathyroid insufficiency. When calcemic doses of vitamin D are given, however, the calcemic effect is added to by increased absorption of calcium. Consequently, and although the calcemic effect of vitamin D may be produced without the feeding of calcium, smaller doses of the sterol may produce the same effect on the serum calcium level if an adequate intake of calcium is provided. The effect of dihydrotachysterol on the absorption of calcium[30] and the fact that this substance is also more effective when given in combination with an increased intake of calcium may be due to its residual antirachitic activity. The effect on absorption of calcium is apparently lacking in the case of solution of parathyroid.[30]

Vitamin D (in calcemic doses), dihydrotachysterol and solution of parathyroid in ascending order,[30] lead to a decided increase in excretion of phosphate by the kidneys, the mechanism of which has recently been studied.[31] The lowered serum calcium in hypoparathyroidism is characteristically accompanied by an increase in the phosphate concentration in the serum. The increased excretion of phosphate through the kidneys, when any of the aforementioned agents is administered, permits a rise in serum calcium with a concomitant fall in serum phosphate while both calcium and phosphate are being added to the blood by liberation of these minerals from the bones. Albright[32] adhered to the view that the fall in serum phosphate actually brings about the mobilization of calcium from the bones, by causing the serum to be less saturated with respect to the bone salt. Von Brand, Holtz and Putschar[33] found the effect of the calcinosefaktor on the serum phosphate level in animals to be quite irregular, a rise in serum phosphate at times following the rise in serum calcium. Hoff[34] found the serum phosphate to rise, following administration of dihydrotachysterol, in contrast to the fall induced by solution of parathyroid.

There is now a considerable literature[35] on the effects of large doses of vitamin D on bone. That Holtz and his co-workers considered this action identical with that of the preparations studied by them is indicated by the fact that they did not study the bones of their animals but referred[33] to the studies of Hoff and Homann[36] on vitamin D as authority for the statement that the calcinosefaktor leads to demineralization of bone. Morris and McLean[37] believe that the effects of the activated sterols on bone result from a direct action on bone tissue. They have found that both calciferol and dihydrotachysterol produce resorption of bone and mobilization of bone mineral and that the latter effect can be visualized as described by McLean and Bloom[38] following administration of solution of parathyroid. These actions are followed by overproduction of new bone, as previously described for both vitamin D and solution of parathyroid,[39] but without the overproduction of fibrous tissue characteristic of hyperparathyroidism (osteitis fibrosa). It is my belief that the calcemic effect of the activated sterols results primarily from a continuous influence of these substances on the interchange of calcium between plasma and bone, resulting in an increased mobilization of bone salt sufficient to keep the serum calcium concentration at higher levels.

Comparative Studies.—It has not been shown by comparative physiologic studies or clinical trial that either calciferol or dihydrotachysterol is superior to the other in the management of parathyroid insufficiency. Throughout the experimental work leading to the introduction of dihydrotachysterol the calcinosefaktor was regarded as common to a variety of substances and of preparations, and it was stated[33] that the action of this

30. Albright, Fuller; Bloomberg, Esther; Drake, T., and Sulkowitch, H. W.: A Comparison of the Effects of A. T. 10 (Dihydrotachysterol) and Vitamin D on Calcium and Phosphorus Metabolism in Hypoparathyroidism, J. Clin. Investigation **17:** 317-329 (May) 1938. Albright, Fuller, and Sulkowitch, H. W.: The Effect of Vitamin D on Calcium and Phosphorus Metabolism; Studies on Four Patients, ibid. **17:** 305-315 (May) 1938.

31. Harrison, H. E., and Harrison, H. C.: The Renal Excretion of Inorganic Phosphate in Relation to the Action of Vitamin D and Parathyroid Hormone, J. Clin. Investigation **20:** 47-55 (Jan.) 1941.

32. Albright, Fuller: Renal Osteitis Fibrosa Cystica, Tr. A. Am. Physicians **51:** 199-212, 1936.

33. von Brand, Theodor; Holtz, F., and Putschar, W.: Vergleichende pharmakologische Untersuchungen über Calcinosefaktor und Nebenschilddrüsenhormone, Arch. f. exper. Path. u. Pharmakol. **167:** 113-145, 1932.

34. Hoff, F.: Untersuchungen über die Wirkung des Präparates, A. T. 10 bei Parathyreopriver Tetanie, Arch. f. exper. Path. u. Pharmakol. **177:** 204-211, 1935.

35. Ham, A. W., and Lewis, M. D.: Hypervitaminosis D Rickets: Action of Vitamin D, Brit. J. Exper. Path. **15:** 228-234 (Aug.) 1934. Raab, H., and Cohn, B. N. E.: Knochenveränderungen bei Vigantol-Vergiftung, Frankfurt. Ztschr. f. Path. **47:** 152-158, 1935. Jones, J. H., and Robson, G. M.: The Effect of Overdoses of Irradiated Ergosterol, Administered for Approximately Two Months, on the Composition and Structure of the Bones of Rats, Am. J. Physiol. **103:** 338-350 (Feb.) 1933. Selye.[39]

36. Hoff, F., and Homann, E.: Zur Frage des Einflusses von Vitamin D und Epithelkörperhormon auf den Kalkhaushalt, Ztschr. f. d. ges. exper. Med. **74:** 258-273, 1930.

37. Morris, W. D., and McLean, F. C.: The Mode of Action of the Activated Sterols on Bone, A Comparative Study, in preparation.

38. McLean, F. C., and Bloom, W.: Mobilization of Bone Salt by Parathyroid Extract, Arch. Path., to be published.

39. Selye, Hans: On the Stimulation of New Bone Formation with Parathyroid Extract and Irradiated Ergosterol, Endocrinology **16:** 547-558 (Sept.-Oct.) 1932.

factor was completely independent of whether the vitamin D activity in the preparations used was destroyed by heating or reduction or not. The nonspecificity of the calcemic effect has again been emphasized by von Werder,[5] and the method used for standardization of dihydrotachysterol, which depends on the toxicity in mice, is in no way capable of distinguishing between the qualitative actions of the various sterols.

Holtz has published no experiments with a preparation identifiable with dihydrotachysterol as now distributed. However, von Brand, Holtz and Putschar [38] compared the actions of various preparations, standardized in terms of their toxicity in mice, and of solution of parathyroid, using a large number of animals of various species. They found numerous differences; in the nature of the pathologic calcification produced, in the curve of the rise and fall of the serum calcium and in the relative susceptibility of the various species to the two substances. They consequently assumed a difference in the mode of action of the sterols and of solution of parathyroid but found, in spite of these differences, that in experimental tetany in dogs, resulting from a deprivation of parathyroid tissue, the action of the parathyroid hormone could be completely substituted for by the calcinosefaktor. In a subsequent paper Holtz, Gürsching and Kraut [40] confirmed these results by observations in man.

Albright, Bloomberg, Drake and Sulkowitch [30] have reported studies of the actions of dihydrotachysterol and of calciferol which have been much quoted. They made comparative studies of the actions of these two substances on the calcium and phosphorus metabolism of 3 patients with parathyroid insufficiency, and a similar study of the action of solution of parathyroid in 1 of these cases. They found that the two sterols have the same two actions of increasing calcium absorption from the gastrointestinal tract and of increasing phosphorus excretion in the urine, the ratio of the latter action to the former being greater with dihydrotachysterol. They noted also that the action of calciferol was slower in coming on and lasted longer than that of dihydrotachysterol. Albright, Sulkowitch and Bloomberg [41] reported similar results in a case of vitamin D-resistant rickets, with the exception that dihydrotachysterol did not cause as marked a rise in excretion of urinary phosphorus. In none of these studies was consideration given to the possibility of a direct effect of the preparations on bone. They gave calciferol at the most in amounts equal to those given of dihydrotachysterol, while for strictly comparable effects the ratio should have been at least 2 to 1.[37]

Himsworth and Maizels [42] treated a patient with congenital hypoparathyroidism for six years, mainly with calciferol. The dosage was maintained, during the greater part of the time, at 12.5 mg. (500,000 international units) a week, with excellent results. During an interim period of ten months dihydrotachysterol was substituted for calciferol. It was effective in controlling the tetany, but the impression of the authors was that "in this patient vitamin D_2 produced a more stable state than did A. T. 10." They used up to 6 cc. a week of the dihydrotachysterol preparation, which should have been equivalent to 60 mg. of calciferol, or nearly five times the dosage of the latter actually employed. Poer [43] has compared dihydrotachysterol and calciferol in the treatment of 11 cases of post-thyroidectomy hypocalcemic tetany. He found that the two substances are equally effective in controlling the symptoms of hypoparathyroidism and in maintaining the serum calcium level near the normal. His usual daily maintenance doses were 1.25 mg. (50,000 international units) of calciferol and 0.3 cc. (1.5 mg.) of dihydrotachysterol. It has not been found by others that this amount of calciferol is usually adequate for a maintenance dose.

Morris and McLean [37] have studied the actions of these two substances in rats. They compared the loss of weight, the mortality, the effects on the bones, as observed histologically, and the onset, distribution and intensity of pathologic calcification in the soft tissues. When given in a ratio of 2.24 mg. of calciferol to 1 mg. of dihydrotachysterol, the loss of weight of litter mates fed the two substances became indistinguishable, and the effects with reference to the other criteria enumerated were also comparable. Using the same dosage ratio, they administered the two substances to dogs. The serum calcium curves showed no significant differences, both substances exhibiting the same ability to raise the serum calcium. From these experiments it is concluded that calciferol must be administered in the ratio of at least 2 mg. to 1 mg. of the basic substance of the commercially available solution of dihydrotachysterol to obtain the same calcemic effect. Others have reported a still higher ratio for the doses necessary to produce comparable toxic effects in mice [40] and in rats [44] (table 1).

Shohl [6] has made comparative studies of the pathologic changes induced in rats by toxic doses of calciferol and of dihydrotachysterol and has found that the two produce similar effects. Both caused striking lesions in the kidneys and blood vessels. Calcification was produced in the gastric mucosa. Both caused demineralization of the bones and overcalcification at the zone of provisional calcification. Neither led to necrosis of the liver produced by an early preparation of irradiated ergosterol,[45] and now believed to be due to its high content of toxisterol.[18]

The comparative studies quoted indicate a qualitative difference between the actions of toxisterol on the one hand and vitamin D and dihydrotachysterol on the other. They fail, however, to disclose any difference in the actions of the two latter substances on which a preference for either one or the other may be based. Further carefully controlled comparative studies, in both clinical and experimental hypoparathyroidism, are required before it can be finally said that calciferol and dihydrotachysterol are of equal value in the management of this condition or that either has advantages over the other.

CLINICAL EXPERIENCE WITH DIHYDROTACHYSTEROL

Of a large number of reports on the use of dihydrotachysterol in hypoparathyroidism, virtually all are unreservedly favorable. In nearly every report the possibility of overdosage is discussed and the necessary

40. Holtz, F.; Gürsching, J., and Kraut, H.: Vergleichende pharmakologische Untersuchungen über Calcinosefaktor und Nebenschilddrüsenhormon, Arch. f. exper. Path. u. Pharmakol. **174:** 51-62, 1933.

41. Albright, Fuller; Sulkowitch, H. W., and Bloomberg, Esther: A Comparison of the Effects of Vitamin D, Dihydrotachysterol (A. T. 10) and Parathyroid Extract on the Disordered Metabolism of Rickets, J. Clin. Investigation **18:** 165-169 (Jan.) 1939.

42. Himsworth, H. P., and Maizels, M.: Vitamins D_2 and D_3 and A. T. 10 in Congenital Thyroid and Parathyroid Deficiency, Lancet **1:** 959-960 (May 25) 1940.

43. Poer, D. H.: Dihydrotachysterol, Parathormone and Vitamin D_2: Comparison of Their Values in the Treatment of Post-Thyroidectomy Hypocalcemic Tetany, South. M. J. **33:** 1174-1180 (Nov.) 1940.

44. Shohl, A. T., and Farber, S.: Effect of A. T. 10 (Dihydrotachysterol) on Rickets in Rats Produced by High Calcium-Low Phosphorus Diets, J. Nutrition **21:** 147-154 (Feb.) 1941.

45. Shohl, A. T., Goldblatt, H., and Brown, H. B.: The Pathological Effects on Rats of Excess Irradiated Ergosterol, J. Clin. Investigation **8:** 505-531 (June) 1930.

precautions are described, but there are few instances of actual toxic manifestations. In a discussion of the first eight years' experience with the preparation, Holtz [28] stated that long-continued administration is without harmful effects and without development of tolerance, that no lasting damage is done if a temporary hypercalcemia of about 15 mg. per hundred cubic centimeters is induced by overdosage and that the danger of toxic effects was overemphasized in the earlier publications. He reported that an occasional patient refractory to dihydrotachysterol was seen. This report of Holtz reflects the general tenor of the large German clinical literature, which will not be reviewed in detail here.

Dihydrotachysterol appears to have been first used in this country by Arnold and Blum,[46] who reported favorably on its effectiveness in 2 cases of postoperative and 1 of idiopathic tetany. Swinton [47] reported favorably on 6 cases of postoperative tetany. MacBryde,[48] from observation of its effects in 6 cases of chronic hypoparathyroidism and 1 of idiopathic tetany, stated that it was the only therapeutic measure in his experience to yield excellent results in treatment of chronic tetany. Pickhardt and Bernhard [49] reported 2 cases of postoperative tetany. Albright, Bloomberg, Drake and Sulkowitch [30] made extensive metabolic studies of 3 cases, concluding that dihydrotachysterol "is a most efficacious therapeutic agent in the treatment of hypoparathyroidism." Rose and Sunderman [25] reported 5 cases of hypoparathyroid deficiency, their observations including determinations of calcium balance, total and diffusible serum calcium, serum protein and inorganic serum phosphorus before and during administration of dihydrotachysterol. They concluded that this preparation is highly effective in increasing the concentration of calcium in the serum and in relieving the symptoms of parathyroid deficiency. In 1 of their cases, following 2 cc. of dihydrotachysterol daily for twenty-six days, severe symptoms of intoxication appeared, including vertigo, tinnitus, thirst, polyuria, nausea and abdominal cramps, with a rise of the serum calcium to 15.7 mg. per hundred cubic centimeters.

Numerous other reports have appeared,[50] the tone of all being favorable and all emphasizing the advantages of dihydrotachysterol over solution of parathyroid in the management of the hypocalcemia associated with parathyroid insufficiency. The reports are virtually unanimous with respect to the details of management. An initial dosage of 1 to 4 cc. daily is commonly continued until the serum calcium level rises to 9 to 10 mg. per hundred cubic centimeters and the symptoms of tetany subside. Following this, individualization of the maintenance dose becomes necessary, and this dose is determined by trial and error. The maintenance dose varies between 0.15 and 1 cc. a day and is more commonly 0.3 to 0.5 cc., but owing to the duration of the action of the substance the required dosage need not be given more often than twice a week. The rise of serum calcium may occur without any addition of calcium to the dietary intake, but the same effect can be obtained with considerably lower dosage of the sterol if the calcium intake is supplemented with from 12 to 20 Gm. daily of a calcium salt, commonly the lactate, chloride or gluconate. The desirability of a low intake of phosphorus is also emphasized.

The most acceptable criterion for regulation of the dosage is frequent observation of the serum calcium level, but the Sulkowitch test, introduced by Albright,[51] appears to be reliable, especially if checked occasionally with determinations of the serum calcium. The test gives a simple and rapid means of detecting or excluding excessive excretion of calcium in the urine, from which the presence or absence of hypercalcemia may be inferred. It has the great advantage that it may be applied daily, or even more frequently, by the patient himself, in much the same way that diabetic patients learn to perform rough quantitative tests for sugar in their urine. According to Goormaghtigh and Handovsky,[17] a serum calcium concentration of 13 mg. per hundred cubic centimeters should be cause for alarm, as it is the prelude to massive calcium excretion, tubular distention and subsequent glomerular regression.

Holtz and Rossmann [52] found that the dose of dihydrotachysterol had to be increased as much as six times during the latter half of pregnancy, and this has been confirmed by Curtis,[26] who gave 3 cc. daily during the last four months of pregnancy, or a dose equivalent to 30 mg. (1,200,000 international units) of calciferol a day. Holtz and Rossmann [53] also found that the dosage of dihydrotachysterol may have to be increased during menstruation and that the effectiveness of a given dose is reduced by the administration of estradiol benzoate. On the other hand, the requirement for dihydrotachysterol is decreased after roentgen castration in women.[53]

Holtz and Kramer [54] have found that larger doses are required during periods of activity, nervous strain and menstruation, and Arnold and Blum [46] have also noted the increased requirement when the patient becomes very active. The variations that are required in dosage with pregnancy and with administration of estrogen are reminiscent of the early observations of the influence of

46. Arnold, C. H., and Blum, H.: The Control of Hypoparathyroidism, West. J. Surg., Obst. & Gynec. **44:** 56-65 (Sept.) 1936.

47. Swinton, N. W.: Postoperative Parathyroid Tetany, New England J. Med. **217:** 165-169 (July 29) 1937.

48. MacBryde, C. M.: The Treatment of Parathyroid Tetany with Dihydrotachysterol, J. A. M. A. **111:** 304-307 (July 23) 1938; South. M. J. **31:** 720-725 (July) 1938.

49. Pickhardt, O. C., and Bernhard, A.: The Treatment of Postoperative Tetany with Dihydrotachysterol, Ann. Surg. **108:** 362-373 (Sept.) 1938.

50. These include:
Greene, J. A., and Swanson, L. W.: Treatment of Hypoparathyroidism, with a Discussion of the Use and Action of Dihydrotachysterol (A. T. 10), J. Iowa M. Soc. **29:** 275-279 (July) 1939.
Hurxthal, L. M., and Claiborne, T. S.: Treatment of Tetany with Dihydrotachysterol (A. T. 10), New England J. Med. **220:** 911-916 (June 1) 1939.
Berk, J. E.: Clinical Experience with Dihydrotachysterol in the Management of Idiopathic Hypocalcemia, Endocrinology **25:** 984-990 (Dec.) 1939.
Blackford, J. M., and Hallenbeck, G. A.: Hypoparathyroidism, Treatment by Dihydrotachysterol, Clinics of the Virginia Mason Hospital, Seattle **19:** 25-29 (June) 1940.
Franco, S. C.: Parathyroid Tetany: Chronic Parathyroid Insufficiency of Ten Years' Duration Successfully Controlled with Dihydrotachysterol, Ann. Int., Med. **14:** 529-532 (Sept.) 1940.
Richards, C. G.: Postoperative Tetany, Rocky Mountain M. J. **37:** 436-440 (June) 1940.
Wilkinson, T. C.: Treatment of Tetany with Dihydrotachysterol, Pennsylvania M. J. **44:** 37-40 (Oct.) 1940.
Newman, H. F.: A Case of Hypoparathyroidism Treated with Dihydrotachysterol, J. Mount Sinai Hosp. **6:** 327-332 (March-April) 1940.
Weber, F. C., Jr., and Richardson, H. B.: Dihydrotachysterol (A. T. 10) and Mineral Metabolism: A Metabolic Study, Endocrinology, to be published.
Margolis and Krause.[78]
Adams.[79]
Ryan.[75]

51. Albright, Fuller: Note on the Management of Hypoparathyroidism with Dihydrotachysterol, J. A. M. A. **112:** 2592-2593 (June 24) 1939.

52. Holtz, F., and Rossmann, E.: Schwangerschaft und Tetanie, Ztschr. f. Geburtsh. u. Gynäk. **116:** 187-199, 1938.

53. Holtz, F., and Rossmann, E.: Ueber Beziehungen der Sexualhormone zum Kalkstoffwechsel und zu den Nebenschilddrüsen, Ztschr. f. Geburtsh. u. Gynäk. **116:** 199-212, 1938.

54. Holtz, F., and Kramer, F.: Ueber Nebenschilddrüsentetanie, Kalkhaushalt, elektrische Erregbarkeit und A. T. 10, Naturwissensch. **24:** 177-182 (March) 1936.

estrus, pregnancy and lactation on the course of experimental parathyroid tetany.[55]

Hypercalcemia and other toxic manifestations of overdosage of dihydrotachysterol are usually managed by withdrawal of the medication, including the calcium added to the intake, by rest in bed and by increasing the intake of fluid. Holtz and Rossmann[53] suggested the administration of large doses of estrogens to combat toxicity, and Seiferth and Kolb[56] reported that the vitamin B complex and vitamin C have a far reaching inhibitory influence on the toxic effects of dihydrotachysterol. They reported that vitamin A increases the toxicity of this sterol, but Morgan, Shimotori and Hendricks[57] stated that a low intake of vitamin A leads to an increase in the damaging effects of toxic doses of vitamin D. None of these antagonistic actions appear to have been given adequate clinical trial in actual poisoning with the activated sterols.

In judging the usefulness of an activated sterol over a long period, consideration should be given to its ability to prevent or to relieve the complications or sequelae of parathyroid insufficiency, as well as to its ability to raise the serum calcium level. Of these, the most troublesome is the occurrence of cataracts. Klemens[58] described the opacities in the lens characteristic of hypoparathyroidism, as seen with the aid of the slit lamp, and stated that a presumptive diagnosis of the nature of the condition can usually be made from the changes in the eye alone. He stated that administration of dihydrotachysterol prevents this condition and as a rule arrests its progress if it has already begun before the preparation is administered. Because there is a widespread impression to the contrary, he emphasizes his statement that no clearing up of already formed opacities of the lens can be expected from administration of dihydrotachysterol. Schmidt-La Baume[59] has reviewed the use of dihydrotachysterol in dermatologic conditions associated with hypocalcemia, more especially in impetigo herpetiformis.

Certain cerebral and psychic symptoms are frequently associated with hypoparathyroidism. They include restlessness, irritability, depression, headache and occasional epileptiform convulsions, of central origin. These and other manifestations referable to the central nervous system are said to be relieved promptly by treatment with dihydrotachysterol. Barr, MacBryde and Sanders[60] reported a case of idiopathic hypocalcemic tetany, associated with increased intracranial pressure and papilledema, together with beginning opacities of the lens. The case responded promptly to treatment with dihydrotachysterol, and the authors suggested that edematous changes in the brain or meninges may occur in hypoparathyroidism more frequently than is recognized and that this factor may be of importance in producing cerebral and psychic manifestations of tetany. Eaton and Haines[61] reported 3 cases of parathyroid insufficiency with symmetrical cerebral calcification, in 1 of which the symptoms were relieved by administration of dihydrotachysterol. They regard symmetrical cerebral calcification, mental deterioration and convulsions as concomitant but not necessarily interdependent cerebral symptoms of hypoparathyroidism.

Dihydrotachysterol has been little used in infantile tetany, and Chu and Sung[62] regarded it as of doubtful advantage in view of the common association of this condition with vitamin D deficiency and rickets. Bloxsom,[63] however, has reported that hypocalcemic tetany in an infant, believed to be of parathyroid origin, was controlled by this sterol, but, it will be noted, in doses large enough to have an appreciable vitamin D activity. Eisenstein[64] has reported a case of tetany in an adult, regarded as "secondary to prolonged intestinal dysfunction," relieved by the administration of dihydrotachysterol. The preparation has also been used in other conditions, even more remote from disorders of the parathyroids. Its use in the treatment of otosclerosis, introduced by Seiferth[65] on the basis of reported slight reduction of serum calcium values in this condition, is stated by Schütz[66] to be without theoretical justification or empirical usefulness.

The American literature is still inadequate with respect to reports of the progress of patients kept under observation and under treatment with dihydrotachysterol over extended periods. It would be desirable to have further reports on some of the cases in which treatment was instituted some years ago.

VITAMIN D IN CLINICAL HYPOPARATHYROIDISM

It will be recalled, from the foregoing discussion of dosage and toxicity, that vitamin D ordinarily has no effect on the serum calcium level unless administered in a daily dosage range of 60,000 to 200,000 international units or even higher and that consequently no effect in the treatment of hypoparathyroidism, comparable to the beneficial effects reported from the administration of dihydrotachysterol, can be expected unless vitamin D is administered at these levels. Irradiated ergosterol was administered in these amounts in the treatment of clinical hypoparathyroidism as early as 1928 with good results,[67] but in most instances the dosage of vitamin D employed has been much below that which is necessary to produce the effects under discussion. The early literature has been reviewed by Boothby and Davis,[68] and many of the unfavorable or equivocal results quoted by them can be clearly traced to insufficient dosage. Except for purposes of comparison, this review will refer only to clinical experience with adequate doses of preparations of vitamin D.

55. Dragstedt, L. R.: The Physiology of the Parathyroid Glands, Physiol. Rev. **7**: 499-530 (Oct.) 1927.

56. Seiferth, L. B., and Kolb, H.: Tierexperimentelle Untersuchungen über die Wirkung der Vitamine A, B and C bei A. T. 10-Vergiftung, Ztschr. f. d. ges. exper. Med. **106**: 167-180, 1939.

57. Morgan, A. F.; Shimotori, N., and Hendricks, J. B.: Progress of Hypervitaminoses D_2 and D_3 and Recovery in Rats, as Affected by Dietary Calcium and Phosphorus and Vitamin A, J. Biol. Chem. **134**: 761-779 (July) 1940.

58. Klemens, F.: Auge und Epithelkörperchen-Unterfunktion, Deutsche med. Wchnschr. **65**: 753-754 (May 12) 1939.

59. Schmidt-La Baume, F.: Die Bedeutung des A. T. 10 für die Dermatologie als Substitutionstherapie bei Hypocalcinosen, Med. Klin. **33**: 1590-1595 (Nov. 26) 1937.

60. Barr, D. P.; MacBryde, C. M., and Sanders, T. E.: Tetany with Increased Intracranial Pressure and Papilledema: Results from Treatment with Dihydrotachysterol, Tr. A. Am. Physicians **53**: 227-232, 1938.

61. Eaton, L. McK., and Haines, S. F.: Parathyroid Insufficiency with Symmetrical Cerebral Calcification: Report of Three Cases, in One of Which the Patient Was Treated with Dihydrotachysterol, J. A. M. A. **113**: 749-753 (Aug. 26) 1939.

62. Chu, T. F., and Sung, C.: Tetany in Infancy and Childhood: A Clinical Study of 45 Cases Seen in North China, with Special Reference to Etiology, J. Pediat. **16**: 607-623 (May) 1940.

63. Bloxsom, A.: Treatment of Tetany of the Newborn Infant with Dihydrotachysterol, J. Pediat. **16**: 344-346 (March) 1940.

64. Einstein, V. W.: Chronic Adult Tetany of Gastrointestinal Origin; Treatment with Dihydrotachysterol: Report of a Case, Pennsylvania M. J. **44**: 33-36 (Oct.) 1940.

65. Seiferth, L. B.: Ueber die Aetiology und Behandlung der Otosklerose, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **143**: 429-455, 1937.

66. Schütz, in discussion on Holtz, F.: Deutsche med. Wchnschr. **65**: 781 (May 12) 1939.

67. Stern, A.: Zur Therapie der parathyreopriven Tetanie mit Vigantol, Deutsche med. Wchnschr. **54**: 1292 (Aug. 3) 1928.

68. Boothby, W. M., and Davis, A. C.: Treatment of Postoperative Parathyroid Insufficiency; An Interpretative Review of the Literature, Arch. Int. Med. **58**: 160-184 (July) 1936.

Bauer, Marble and Claflin [69] reported in 1932 on 3 cases of hypoparathyroidism in which irradiated ergosterol was administered in doses of 5 mg. a day. The preparation was that responsible for much of the confusion concerning toxicity of vitamin D. Beneficial results were observed in all 3 cases, but only when the calcium intake was adequate. Reed and Seed [70] reported in 1933 on the treatment of 10 cases of parathyroid tetany in which viosterol was administered in doses up to 920,000 international units a day over periods of several days. Reed, Struck and Steck [15] reported on the subsequent history of these patients, together with 5 more whose treatment was initiated after publication of the original report. In 1939 all but 5 of the 15 patients in the series had been able to discontinue vitamin D therapy without recurrence of tetany. Of these 5, 4 had continued the treatment for six or seven years but were able to secure freedom from tetany on approximately one tenth of the dosage required at first, and without recourse to calcium.

Freyberg, Grant and Robb [71] emphasized the necessity for large doses if satisfactory results from the administration of vitamin D in hypoparathyroidism are to be expected. They gave as much as 200,000 international units of vitamin D as viosterol a day, with definite benefits, but most of the time used from 20,000 to 40,000 units. Stacey [22] gave up to 8 mg. (320,000 international units) of calciferol a day, with favorable results. Himsworth and Maizels [42] reported a case in which calciferol was given for six years, with excellent results. For the greater part of this time the dosage was maintained at 12.5 mg. (500,000 international units) a week. During one period vitamin D_3 was substituted for calciferol (vitamin D_2), with identical results. Farquharson [72] undertook to find the smallest daily dose of irradiated ergosterol that would relieve the symptoms of 2 patients suffering from severe chronic postoperative tetany refractory to other forms of treatment. One of these patients became free from tetany and remained well for four and one-half years with a daily dose of 94,000 international units of vitamin D. In another patient, with the same dose, favorable results were obtained, the symptoms of tetany recurring when the medication was discontinued. Klatskin [73] made a careful study of 2 cases of chronic parathyroid tetany, giving calciferol in doses up to 7.5 mg. (300,000 international units) a day, without the occurrence of toxic manifestations. He recommended calciferol "as a valuable therapeutic agent in cases of chronic parathyroid tetany which do not respond to high calcium-low phosphorus diets and in whom satisfactory transplants of parathyroid gland are not possible." Poer [43] has used calciferol, in doses of 1.25 mg. (50,000 international units) a day, with effects comparable to those seen with dihydrotachysterol. Anderson and Lyall [74] found that the minimum dose of vitamin D necessary to raise the serum calcium to a normal level in parathyroid deficiency appears to lie between 30,000 and 40,000 international units a day.

Of especial interest, in view of the conclusions in this review, are the reports in which vitamin D preparations are compared unfavorably with dihydrotachysterol. Table 2 summarizes data derived from five such reports [75] and includes the dosage of dihydrotachysterol required to produce the desired effect and the maximum dosage of vitamin D which failed to produce this effect. The latter is compared with the dosage of vitamin D calculated to be equivalent in "calcemic principle" with the dosage of dihydrotachysterol.

It is at once apparent from table 2 that the chief source of the unfavorable comparisons made by the authors of these reports is a misapprehension as to what constitute doses of vitamin D comparable to those of dihydrotachysterol. In three of the five reports the doses of vitamin D are 10,000 international units a day or less, or within an entirely different dosage range from that required to raise the serum calcium level. MacBryde [48] used up to 40,000 international units a day, or doses on the borderline of those found by others to be effective in the treatment of parathyroid insufficiency, but gave no further details. In the single case reported by Adams [76] he gave 120,000 international units of vitamin D daily for two weeks during subacute tetany five weeks after thyroidectomy, or an amount which ordinarily should have been sufficient to produce the calcemic effect. After two weeks of this treatment the symptoms continued unabated and the serum calcium remained at about 5 mg. per hundred cubic centimeters. After two weeks of treatment with 2 cc. of dihydrotachysterol (equivalent in calcemic principle to 800,000 international units of vitamin D) daily, the serum calcium rose only to 6.8 mg. per hundred cubic centimeters, but the symptoms were relieved. Two and one-half months later the patient was discharged on a maintenance dose of 1 cc. of dihydrotachysterol twice a week. It appears that during the acute or subacute stage of her tetany this patient was resistant to both vitamin D and dihydrotachysterol and that sufficient dosage only of the latter was given.

TABLE 2.—*Summary of Reports Favorable to Dihydrotachysterol and Unfavorable to Vitamin D*

Authors	Dihydrotachysterol: Daily Dose Giving Favorable Effect, Cc.	Vitamin D: Equivalent to Dihydrotachysterol, Units	Vitamin D: Maximum Actually Given, Units
Margolis and Krause [75]	1.0	400,000	1,700
Ryan [75]	0.5	200,000	3,000
Curtis [26]	1.0	400,000	10,000
MacBryde [48]	0.25-1.0	100,000-400,000	40,000
Adams [76]	2.0	800,000	120,000

It would appear that there is no reason to attribute a higher degree of specificity or a lesser likelihood of toxicity to dihydrotachysterol than to vitamin D.

69. Bauer, Walter; Marble, Alexander, and Claflin, Dorothy: Studies of the Mode of Action of Irradiated Ergosterol, J. Clin. Investigation **11:** 47-62 (Jan.) 1932.

70. Reed, C. I., and Seed, L.: The Treatment of Clinical Tetany with Irradiated Ergosterol, Endocrinology **17:** 136-148 (March-April) 1933.

71. Freyberg, R. H.; Grant, R. L., and Robb, M. A.: Hypoparathyroidism: The Treatment of Chronic Cases, J. A. M. A. **107:** 1769-1775 (Nov. 28) 1936.

72. Farquharson, R. F.: Hypoparathyroidism and Tetany, Univ. Toronto M. J., November-December 1938.

73. Klatskin, G.: On the Actions of Crystalline Vitamin D_2 (Calciferol) in Chronic Parathyroid Tetany, J. Clin. Investigation **17:** 441-443 (July) 1938.

74. Anderson, I. A., and Lyall, A.: Treatment of Chronic Hypoparathyroidism, Quart. J. Med. **8:** 209-232 (July) 1939.

75. Margolis, H. M., and Krause, Gilbert: Postoperative Parathyroid Tetany, Complete Control of the Manifestations by Means of Dihydrotachysterol: Report of a Case, J. A. M. A. **112:** 1131-1133 (March 25) 1939. Ryan, E. J.: The Treatment of Postoperative Parathyroid Tetany; Use of Dihydrotachysterol (A. T. 10), M. Clin., North America **24:** 443-449 (March) 1940. Curtis.[26] MacBryde.[48] Adams.[76]

76. Adams, L. J.: Postoperative Tetany Treated with Dihydrotachysterol (A. T. 10), Canad. M. A. J. **42:** 373-375 (April) 1940.

That doses of the latter sufficient to produce effects comparable to those of dihydrotachysterol can be given with at least the same degree of safety, provided the same precautions are observed, is established. There is needed, however, a larger volume of clinical experience with vitamin D comparable to that accumulated for dihydrotachysterol.

COMMENT

The present review emphasizes my point of view that the burden of proof is on those who would maintain that dihydrotachysterol is a better or safer agent in the treatment of hypoparathyroidism than is vitamin D. This statement does not in any way detract from the proved effectiveness, usefulness and comparative safety of dihydrotachysterol. It seeks merely, and on the basis of the available evidence, to put vitamin D in the same category with respect to the same physiologic actions and therapeutic usefulness.

The present favor in which dihydrotachysterol finds itself, in comparison with the disfavor or relative indifference to vitamin D, appears to have arisen from the following considerations: First, the earlier trials of vitamin D were mainly with inadequate dosage, and comparisons are still made between antirachitic doses of vitamin D and full calcemic doses of dihydrotachysterol. Second, the early experience with toxic preparations of irradiated ergosterol, resulting from their high content of toxisterol, led to a fear of poisoning with overdoses of vitamin D, a fear which has not been supported by the experience of the past few years. Third, the standardization of vitamin D products in terms of antirachitic units leads to the expression of dosages adequate for the management of hypoparathyroidism in terms of tens or hundreds of thousands or even of millions of units. With a background of fear of overdosage, the physician faces the psychologic barrier of having to prescribe what appear to him to be enormous, and frequently described as "massive," doses of a toxic preparation.

All these handicaps have been removed in the case of dihydrotachysterol. Although its toxic, and therapeutically effective, principle appears to be identical with that of vitamin D, it was introduced without the same fear of toxic effects. Its dosages are expressed in the innocuous terms of cubic centimeters, and even when "toxic borderline doses" are referred to the dosage is in hundreds rather than in millions of units. Moreover, it was introduced for one purpose only and has been given publicity only for this purpose. Without any direct claim to this effect having been made, the impression has become widespread that its action is specific, and in the current literature [77] it is even referred to as "a new form of parathyroid hormone."

It is my belief, from the evidence available at present, that preparations of vitamin D are as effective and as free from danger as is dihydrotachysterol. More clinical experience is needed, and a system of standardization and of dosages free from the present handicaps to the use of vitamin D for the purposes here discussed is required. For pure vitamin D_2, or calciferol, dosage should be expressed in milligrams. Preparations of irradiated ergosterol should be standardized in terms of their content of the calcinosefaktor, which will include the activity of the tachysterol content. The method of Holtz, Laquer, Kreitmair and Moll [10] is probably suitable for this purpose. The physiologic activity, in terms of the toxic factor, should then be referred back to pure calciferol rather than to arbitrary "toxic borderline units." A rough calculation, assuming that irradiated ergosterol contains about 25 per cent tachysterol, indicates that average viosterol should have about 16 per cent more calcemic activity than is indicated by its content of vitamin D_2.

It now seems that the dangers of administration of both dihydrotachysterol and of vitamin D have been somewhat exaggerated. They must be administered with care and with the proper precautions, but the immediate dangers are apparently no greater than in the case of insulin. Frequent determinations of serum calcium are desirable not only during the initial stages but also after maintenance doses have been arrived at. The Sulkowitch test,[51] by which the excretion of calcium into the urine is observed by a simple and roughly quantitative method, may serve to avoid the necessity for frequent examinations of the blood.

That prolonged administration of these products will lead to chronic injury in man has not been shown, nor is it clear that the danger does not exist. The effects on the arteries and arterioles of dogs have been referred to. In any case the possibility of such danger must, in cases of hypocalcemia resulting from hypoparathyroidism, be weighed against the very probable occurrence of opacities of the lens, and perhaps of other sequelae of this condition. At present the evidence is that the risk of injury from the therapeutic agent is far less than that from the condition which it is intended to combat.

Finally, I wish to enter a plea for the abandonment of the term "hypervitaminosis D." Not only is the term misleading and nondescriptive but it is also a deterrent to the legitimate and desirable use of vitamin D products in the treatment of hypocalcemia. The term "vitamin D," without further qualification, refers solely to the antirachitic activity of the activated sterols, although "vitamin D_2" and "vitamin D_3" are now used to refer to specific chemical substances. Since the toxic effects from administration of vitamin D products are shared with other products having little or no vitamin D activity, it is clear that the characteristics of the sterol molecule responsible for its antirachitic activity are not those responsible for the toxic effects. There is no evidence that overdosage with the antirachitic factor per se leads to any undesirable effects. For these reasons the toxic actions of the activated sterols should be separated from their antirachitic activity in terminology as they are in fact.

SUMMARY

1. A number of substances derived from activation products of ergosterol and cholesterol have the effect of raising the serum calcium when administered in sufficiently large doses, this effect resulting from a combination of the mobilization of calcium from the bones and an increase in absorption from the gastrointestinal tract. Of these, only vitamin D_2 (calciferol)

77. Slaughter, E. C.: Experimental Hyperparathyroidism and Otosclerosis, Ann. Otol., Rhin. & Laryng. **49**: 130-140 (March) 1940.

and dihydrotachysterol (also known as A. T. 10) have been extensively used clinically.

2. Because of this effect on the serum calcium, here called the "calcemic effect," both of these substances are highly effective in increasing the concentration of calcium in the blood and in relieving the symptoms resulting from hypocalcemia in cases of insufficiency of the parathyroid glands. The substances may be administered by mouth over considerable periods of time and with reasonable safety, provided proper precautions are observed. Their prolonged use is attended neither by injury to the patient nor by the development of tolerance.

3. When the two substances are administered in comparable doses their effects are qualitatively and quantitatively similar, if not identical. It has not been shown that either is superior to the other in the management of hypoparathyroidism. Previous unsatisfactory experience with vitamin D products has been due either to insufficient dosage, in which case no beneficial results were obtained, or to the effects of a widely used preparation containing the toxic products of overirradiation.

4. The dangers of the toxic effects of these substances in the preparations now available, while real, have been somewhat overemphasized. Frequent determinations of serum calcium are desirable both to determine that the desired elevation has been obtained and to avoid the dangers of hypercalcemia. The Sulkowitch test, by which the excretion of calcium into the urine is observed and which the patient himself learns to perform, serves to permit close observation and at the same time to reduce the frequency of the necessary blood examinations.

5. While the possibility of chronic injury resulting from prolonged administration of these substances has not been excluded, such injury has not been demonstrated. At present the evidence is that the risk of injury from the therapeutic agent is far less than that from the condition it is intended to combat.

6. The "calcemic principle" responsible for the elevation of serum calcium and for the toxic actions of the activated sterols has been dissociated from the antirachitic activity of certain of these sterols. In the case of vitamin D the antirachitic activity and the calcemic action are apparent in widely separated dosage ranges. Confusion as to dosage and the expression of calcemic doses in terms of tens or hundreds of thousands of units have been handicaps to the use of vitamin D in the management of hypocalcemia.

7. It is urged that these handicaps be removed by the expression of dosages for the calcemic effect in terms of weight of calciferol. In the case of viosterol, which contains other substances with the same action but not accounted for in the standardization of this preparation in terms of antirachitic activity, the calcemic effect should be determined by biologic standardization and referred back to pure calciferol.

8. The term "hypervitaminosis D" should be abandoned. The term is misleading and nondescriptive and is a deterrent to the legitimate and desirable use of vitamin D products in the treatment of hypocalcemia.

951 East Fifty-Eighth Street.

Council on Physical Therapy

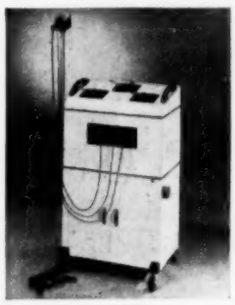
THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

BURDICK SU-4 ELECTROSURGICAL UNIT ACCEPTABLE

Manufacturer: The Burdick Corporation, Milton, Wis.

The Burdick SU-4 Electrosurgical Unit provides a means of applying the various technics used in surgical diathermy. Two currents, one of which is from a spark gap high frequency generator and the other from a vacuum type oscillator, are supplied. For cutting, the tube current alone or a blend of the two currents is used, and the current from the spark gap generator is used alone for coagulation. Standard accessories furnished with the unit include an electrode handle with cork and attachment plug, silver indifferent electrode, small and large size ball coagulation electrodes, needle for cutting or coagulation, tungsten knife blade and straight knife blade for dissection, set of five long needles and ball electrodes for coagulation, and an instrument rack.

Mounted on a steel chassis, the unit is contained in a steel cabinet having a white enamel finish. A lower section of the cabinet provides storage space for the foot switch, cords and accessories. A removable instrument tray is supplied with the apparatus.



Burdick SU-4 Electrosurgical Unit.

The standard type spark gap circuit has a high voltage condenser with heat dissipating cast aluminum mountings connected across the transformer secondary. A WL-460 tube is used in the Hartley circuit with parallel feed plate supply, using alternating current for its anode voltage, and is isolated from the spark gap oscillator and blending circuit by variable magnetic coupling. Five line voltage adjustments are provided by a line transformer.

The blending circuit contains a coil capacity coupled to the spark gap circuit and magnetically coupled to the tube circuit, being common to these two generating circuits. The patient circuit is capacity coupled to this coil. Since the two generating circuits operate without appreciable influence on each other and either generator will feed the patient outlet alone, the output blended current is the sum of their individual outputs. The parallel connection of circuits is a feature; according to the firm, with this connection the ratio of between the spark gap oscillator component in the blended current remains constant with varying patient impedance and current. A separate circuit and outlet provided for large electrode coagulation disconnects the spark gap circuit from the blending circuit.

Three controls on the operating panel consist of a six position master switch, a dissection power control regulating the amount of current from the spark gap generator. Each component of the blended current can be separately controlled. The foot switch has two pedals; the one marked "Coagulation" turns on the spark gap generator. When the master switch is set on "Blended Current," the "Dissection" pedal of the foot switch turns on the two generators simultaneously, producing the blended cutting current.

The unit was investigated clinically by the Council and was found to give satisfactory service.

The Council voted to accept the Burdick SU-4 Electrosurgical Unit for inclusion on its list of accepted devices.

Aretaeus Anticipated Kraepelin.—Aretaeus (30-90 A. D.), a clinician of the second century, described the aurae of epilepsy, differentiated senile and involutional states, and seems to have been the first to propose the clinical concept of "circular psychoses." He anticipated Kraepelin by eighteen hundred years in his manic-depressive theories.—Lewis, Nolan D. C.: A Short History of Psychiatric Achievement, New York, W. W. Norton & Co., Inc., 1941.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, AUGUST 23, 1941

ALLEGED TYPHOID ULTRAVIRUS

Among the basic medical researches interrupted by the war, Magrassi's [1] introductory studies of the toxicity or pathogenicity of the dissociable "Vi antigen" of Eberthella typhosa are of peculiar interest. Ordinary laboratory strains of the typhoid bacillus differ from freshly isolated cultures, as was demonstrated nearly fifty years ago by Sanarelli.[2] He found freshly isolated bacilli highly toxic for guinea pigs and mice and incapable of agglutination with antityphoid serum. Both the toxicity and the inagglutinability, however, are rapidly decreased and eventually lost on subculture. Sanarelli concluded that toxicity, virulence or pathogenicity are nonessential characters of the typhoid bacillus, which may be gained or lost by proper environmental exposure. The typhoid bacillus, according to this view, was a nonpathogenic mechanical carrier of some unknown autocatalytic toxic enzyme in about the same way that it is now conceived to carry bacteriophage.

Sanarelli's discredited theory was reformulated by Felix and Pitt [3] about forty years later. They found that in addition to the well recognized flagellar and somatic antigens a third antigen is present in freshly isolated strains of E. typhosa. This third antigen gradually decreases in amount and eventually disappears on subculture, its decrease being parallel with loss of toxicity or virulence. Felix and Pitt therefore suggest that this third antigen should be known as the "virulence factor" or "Vi antigen."

Numerous investigators have shown that this Vi antigen is readily dissociable from the typhoid bacillus. By incubating a freshly isolated saline suspension of E. typhosa for four hours, the Vi factor is set free in the suspension fluid and may be separated from the formed elements by high speed centrifugation or Chamberland filtration. The highly toxic filtrate thus obtained is readily inactivated by heating to 60 C. for thirty minutes.

Friedberger [4] had said that a dissociable toxic factor plays a role in clinical typhoid. Aqueous extracts of the organs of patients dying of typhoid were found to be highly toxic for guinea pigs. The brains of guinea pigs killed during the acute febrile reaction to this tissue toxin will transfer the toxic symptoms to normal guinea pigs, and brain to brain transfer of typhoid "endotoxin" could be continued indefinitely without appreciable loss of virulence. Friedberger concluded from this serial transfer that the etiologic factor in typhoid is a double "entity," a microscopically visible and culturable typhoid bacillus supplemented by an invisible, noncultivable autocatalytic "cryptic antigen." In today's terminology this "cryptic" antigen would be classed as an ultravirus.

This "binomial" theory of typhoid was received with universal skepticism twenty years ago. Following the development of modern theories of synergic virus-bacterial infections (e. g. swine influenza), however, experimental verification of the Friedberger concept was undertaken by Italian investigators. Sanarelli and Alessandrini,[5] for example, attempted to disprove the theory by showing that Friedberger's alleged synergic ultravirus is nothing more than an invisible phase of E. typhosa. In this they were unsuccessful, as regeneration of the typhoid bacilli was not possible from the invisible toxic filtrate.

Friedberger's synergic theory was therefore tentatively accepted as a working hypothesis by the Italian investigators. Magrassi and his co-workers [1] of the Institute for General Clinical Medicine, University of Rome, confirmed Friedberger's basic experiments. Substituting baby rabbits for the more resistant guinea pigs of previous experiments, they found that a Chamberland filtrate of partially autolyzed virulent E. typhosa is highly toxic. Injected intraperitoneally or intravenously in 4 to 8 cc. doses of standard dilution (200 million E. typhosa organisms per cubic centimeter) the Vi antigen produces diarrhea, muscular weakness and rapid loss of weight with an occasional death within twenty-four hours. Most of the rabbits, however, soon recover from the initial symptoms following injection and remain apparently normal for from eight to twelve days. At the end of this latent period a recurrence of the diarrheal symptoms develops. The rabbits usually lose a third of their original weight before death, which usually occurs in from two to three days. An occasional animal may survive as long as ten to thirty days. Magrassi found that the initial toxic reaction could be avoided by reducing the dose of the filtrate to 0.5 cc. injected intracerebrally. The terminal fatal emaciating

1. Magrassi, F., and Galli, F.: Boll. r. Acad. med. di Roma **64:** 7, 1938. Magrassi, F.; Galli, F., and Scalfi, L.: Arch. f. ges. Virusforsch. **1:** 324, 1940.

2. Sanarelli, G.: Ann. Inst. Pasteur **6:** 721, 1892.

3. Felix, A., and Pitt, R. M.: J. Path. & Bact. **38:** 409 (May) 1934.

4. Friedberger, E., and Meissner, G.: Klin. Wchnschr. **2:** 449 (March 5) 1923. Friedberger, E., and Cecchini, A., ibid. **2:** 2345 (Dec. 24) 1923.

5. Sanarelli, G., and Alessandrini, A.: Ann. d'ig. **42:** 129 (March) 1932; **43:** 621 (Sept.) 1933.

diarrhea after a latent period of eight to twelve days is the only toxic manifestation by this method of injection.

On necropsy a great majority of the intracerebrally injected rabbits yielded heart blood, brain, spleen and liver that were bacteriologically sterile, colon bacilli being the only occasional contaminant. Confirming Friedberger's discredited data, Magrassi found that 0.5 cc. of a 10 per cent aqueous extract of the brains at necropsy would reproduce the fatal emaciating diarrhea if injected intracerebrally into normal rabbits and that this brain to brain transmission of the autocatalytic toxic factor could be continued for at least six generations, the highest number of passages attempted by the time of the interruption of his work.

The possibility that this apparently successful transfer of typhoid encephalitis might be due to some latent neurotrophic virus was eliminated by the Italian investigators, who did numerous control tests. Heat inactivated Vi antigen, autolysates of avirulent strains of E. typhosa and 10 per cent extracts of normal rabbit brains would not reproduce the disease. Magrassi found also that the heart blood of the rabbits which were subjected to such passage almost invariably contained typhoid agglutinins of relatively high titer (e. g. 1:400 to 1:12,800), a specific antibody production that could hardly be expected from an unknown contaminant.

A second constant finding in the rabbits with typhoid encephalitis was a massive overgrowth of colon bacilli in the small intestine. This led to the belief that the hypothetical typhoid ultravirus is capable of "activating" or "energizing" normal intestinal saprophytes, conferring on them a distinct toxicity or pathogenicity. This overgrowth led the Italian investigators to believe that the terminal emaciating diarrhea in typhoid encephalitis is due to "Vi activation" of colon bacilli.

Attempts to measure the size of this hypothetical typhoid ultravirus, its cultivation on modern virulogic mediums and its possible infectivity on intranasal instillation were not completed at the time of the discontinuation of this work. Magrassi, however, feels justified in concluding from his interrupted data that a highly pathogenic ultravirus can be dissociated from freshly isolated virulent typhoid bacilli, that this dissociated virus is capable of independent multiplication in the brain and other tissues of baby rabbits, and that so grown the ultravirus is capable of directly or indirectly "activating" the normal intestinal flora, conferring a lethal toxicity on it.

Friedberger's discredited synergic theory of typhoid infection has therefore apparently received sufficient experimental confirmation to warrant serious reconsideration.

THE PATIENT COMES FIRST

Hardly half a century has passed since hospitals for the treatment of private patients were first established. Previously hospitals were maintained for the benefit of those who were destitute. Obviously such hospitals depended for their support on public appropriations or on voluntary gifts. Services of the physician were freely contributed without thought of compensation. Asepsis, which made possible elective operations, and a radical change in our domestic economy, initiated fundamental changes in the situation. Now all classes of society have become accustomed to resort to the hospital both for diagnosis and for treatment in minor as well as in major illnesses. The hospital today frequently derives a part, sometimes all, of its income from paying patients. Increasingly hospitals sell their services to the self-supporting members of society.

This transformation of the economic status of the hospital has not been achieved without evidences of maladjustment, as emphasized by Dr. Miles Atkinson [1] in the *Atlantic Monthly*. Amidst the complexities of organization and administration, he says, we have lost sight of the fact that hospitals exist primarily for the benefit of the sick. The doctor occupies the second place in importance. Without him and the patient there would be no need for the hospital. Building and equipment are needed to aid the physician to apply his knowledge and skill in the treatment of the sick. The hospital and its administrators, then, take only the third place in the medical economy, a fact too often overlooked, so that the hospital organization becomes an end in itself, to the detriment of patient and staff. The present crisis, according to Dr. Atkinson, is due at least in part to the lavish expenditures of the postwar era, which have left us a legacy of costly buildings, heavy mortgages, needless equipment and unnecessary personnel. The notion that aggregations of institutions would simplify management or effect economies has proved to be a delusion. "A hospital is not a factory." Patients cannot be treated *en masse*. One of the evils of unduly expanded institutions is excessive specialization.

Private hospitals in recent years, by reason of diminishing income from endowment and from subscriptions, have resorted to the policy of charging in the lower income brackets whatever the traffic will bear. Unforeseen consequences of this policy have been the exploitation of the patient and of the doctor as well. Too often the roentgen ray department and laboratories have been operated for profit. The same may be true of the pharmacy. In either case the patient and the public suffer, as well as the physician and pharmacist.

Dr. Atkinson concludes that hospitals are abusing their position. Nobody cavils at the work they do, but many cavil at the means they adopt to do it. The hospitals, he believes, are in a parlous state, and something very soon will have to be done about it.

1. Atkinson, Miles: The Patient Comes First, Atlantic Monthly, August 1941.

Current Comment

ESSENTIAL FRUCTOSURIA

Essential fructosuria is a rare anomaly of metabolism, apparently harmless but sometimes mistaken for diabetes. It is characterized by inability to utilize fructose completely. The disturbance is manifested by the presence of fructose in the urine in amounts proportional to the quantity of sugar ingested. Because of its rarity it has been difficult to speculate convincingly concerning the etiology. Now however Lasker,[1] by adding 7 new cases to the literature and analyzing them as well as the 40 previously reported, is enabled to demonstrate a familial occurrence. Although the evidence for inheritance of this disturbance is not yet conclusive, its occurrence in sibs, its nonoccurrence in the parents and offspring of persons with fructosuria, and the frequency of consanguininity of parents of such persons all offer evidence to indicate that fructosuria is inherited as a mendelian recessive characteristic. Final confirmation of this theory may be long in coming, however, since additional evidence can be accumulated only slowly because of its rarity.

BIOTIN IN TUMOR TISSUE

The search for biochemical differences between normal and tumor tissue is being continued by investigators with the hope that the presence of an abnormally low or unusually high concentration of a particular substance in tumor tissue may be a clue to some aberration in the metabolism of living tissue which is responsible for the neoplasm. Of particular interest are substances of vitamin or enzyme nature which, as components of catalytic systems, exert a profound regulatory effect on the rate of metabolic processes. Biotin, or "vitamin H," is one of the more recently studied of these compounds and is said to exert a catalytic influence in minute concentrations. This substance is essential for the normal function of many micro-organisms and also for higher animals. In a recent preliminary communication, West and Woglom [1] report observations on the relative abundance of this growth factor in various tissues, including certain tumor tissues. In the case of every type of tumor studied, with one exception, the biotin content of the tumor was found to be distinctly higher than the concentration of this vitamin in control normal tissue of the same type. In rats with primary carcinoma of the liver induced by feeding butter yellow, the biotin level of the liver adjacent to the neoplasms was found to be normal, while the carcinomas themselves, unlike the other tumors analyzed, were distinctly lower in their biotin content. In every case studied the biotin level of the tumor deviated sharply from the normal adult values in the same direction as that of the corresponding embryo tissues. This relationship appears to be a difference in metabolism shared by tumor and embryo rather than a change common to all rapidly dividing tissue, as the biotin content of rat liver vigorously regenerating after partial hepatectomy or of the pregnant human uterus was not found to differ from that of the same tissues in a nonhyperplastic state. It has been further suggested by Laurence [2] that both malignant cells and micro-organisms which have been found associated with the observed cases of spontaneous recession of tumors require excess biotin for their metabolic activities. If this hypothesis is correct, the spontaneous recessions might be explained as the direct result of biotin deficiency brought about by the avidin-like action of the micro-organisms, thus depriving the malignant cells of a factor vital for their continued existence. (Avidin is a special constituent from raw egg white, which has a biotin-binding capacity in vitro.) Whether or not this theory can be confirmed, the discoveries already made have opened a new line of investigation on the physiology of tumors.

ORAL ANDROGENIC THERAPY

Physicians have been recently advised of the availability of an androgen which is far more potent, orally, than the testicular hormone testosterone. This substance, methyl testosterone, has been shown to be as effective orally as one third to one fourth the amount of injected testosterone propionate necessary for adequate replacement therapy in eunuchoid or castrate animals. The biochemists who first prepared this material have indeed made a noteworthy contribution to endocrinology. Nevertheless, physicians should not readily accept the extravagant therapeutic claims made by the firms which are marketing this substance (Schering, Roche-Organon and Ciba) or the urge to prescribe methyl testosterone as an economical and practical form of medication. The Council on Pharmacy and Chemistry has declared, in a report on the status of testosterone propionate, that final judgment of androgenic therapy must await additional evidence and that the only worthwhile indication for this therapy at present seems to be its application in the treatment of eunuchoidism or castration in the male. The other indications for androgenic therapy should be subjected to further investigation. In the light of this report, the indications for methyl testosterone should be scrutinized carefully. Furthermore, relatively large amounts of methyl testosterone are essential for effective therapy. On the basis of available reports, it is necessary to administer 50 to 100 mg. of this material daily for complete replacement therapy in the castrate. Physicians should therefore contemplate the economic aspects of administering such doses over the appropriate period of time. Actually reports dealing with the use of methyl testosterone in such conditions as menstrual disorders, painful breasts, menopausal symptoms and prostatism are meager and quite inconclusive.

1. Lasker, Margaret: Essential Fructosuria, Human Biol. **13**: 51 (Feb.) 1941.

1. West, P. M., and Woglom, W. H.: Science **93**: 525 (May 30) 1941.

2. Laurence, William L.: Induced Biotin Deficiency as a Possible Explanation of Observed Spontaneous Recessions in Malignancy, Science **94**: 88 (July 25) 1941.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

THE PREHABILITATION OF REGISTRANTS

V. A UNIVERSITY PROGRAM TO PREPARE STUDENTS FOR MILITARY SERVICE

RUTH E. BOYNTON, M.D.
AND
HAROLD S. DIEHL, M.D.
MINNEAPOLIS

The administration of the University of Minnesota believes that higher educational institutions have not only an opportunity but also an obligation to prepare their students for the parts which they will be called on to play in the national defense program. University departments concerned with health, physical fitness and recreation are in a position to utilize their resources in equipment, buildings and personnel to render a special service to the men who will be selected for military training. With this in mind, during the spring quarter of 1941 an experimental program was planned and carried out for the prehabilitation of university students registered under the Selective Training law.

This program consisted of (1) registration of all men in the university to determine their status in regard to Selective Service, (2) a complete medical examination according to the physical standards of the Selective Service Act, (3) an examination to determine the physical strength and endurance of these students, (4) a written examination to give information of the recreational interests and skills of these men, (5) a comprehensive examination in personal hygiene and public sanitation, with special attention to requirements of army life, and (6) the development of a program based on information gained in these tests which would enable all students needing remedial work or special classes to obtain them.

REGISTRATION

The only part of this program which was compulsory was the registration of all male students in the university. A card was sent to each male student asking for information on age, whether registered for Selective Service, and if so registered his classification (if any), his Selective Service numbers, and whether he expected an early or late call for Selective Service. Such information cards were sent to over nine thousand male students. Of this number 46 per cent replied that they had registered for Selective Service. In certain colleges with older students the percentage registered for Selective Service was naturally much higher. For example, in the Graduate School 92 per cent of the students were registered, in Medicine 87 per cent and in Dentistry 76 per cent, whereas in the College of Science, Literature and the Arts only 26 per cent of students were of draft age.

Of those students registered for Selective Service, one thousand, two hundred and sixty-eight either had low call numbers or signified their wish to participate in the prehabilitation program, although they did not expect an early call.

From the University of Minnesota.

MEDICAL EXAMINATIONS

The medical examinations were given during the spring vacation and in the evening of the first week of the spring quarter to make it possible for students to have examinations without interfering with their class work. The examinations were carried out according to the physical examination standards set up under the Selective Service Act. On completion of the examination each student was classified according to Selective Service standards as follows: class I-A, fit for general military service; class I-B, fit for limited military service; class 4-F, unfit for any military service.

Nine hundred and twenty-nine students were given medical examinations. The classifications of these according to the physical standards of the Selective Service Act were as follows: class I-A, 599, or 64 per cent; class I-B, 199, or 21 per cent; class 4, 79, or 8.5 per cent; classification deferred pending further study, 52, or 6.5 per cent. Over one half of the 52 whose classification was deferred will be put in class I-A. Approximately 30 to 33 per cent of the group will finally be classified either as class I-B or class 4. This percentage is approximately the same as that found among the men in this vicinity already inducted into military service under the Selective Service Act.

Table 1 lists the major causes for restricted classification with the percentage rejected for unlimited service for each cause. Although the total percentage of university students classified as 1-B or class 4 is approximately the same as for the draftees who have been examined by the Selective Service examiners, the causes for restricted classification differ from the findings of the draftees examined in Minnesota. A report on the physical examination of 17,337 Minnesota registrants for Selective Service who were examined during January 1941 is available. Of this number 33 per cent were put in class 1-B or class 4. A comparison of the defects which caused disqualification for these draftees with the defects found in University of Minnesota students is given in table 2.

The two striking differences between the groups are the high percentage of college students given restricted classifications because of visual defects and the low percentage of college students given restricted classifications because of defective teeth. The large majority of students with restricted classifications because of visual defects were myopic. All cases so classified had the myopia corrected by glasses. The 7 per cent of the group who were restricted in classification because of underdevelopment were those who were either underweight or under the required height or whose chest measurements did not meet the standards set under the Selective Service regulations. Many of the young men in this group could reach the standards set by a proper program of diet, rest and exercise.

It is worthy of note that the large majority of university students who were given restricted classifications because of physical defects had defects of a character which are not correctible so far as army service is concerned. All students whose physical defects are remediable are being followed up and arrangements are being made for the correction of these defects through the student's private physician or through the Health Service.

TABLE 1.—*Causes for Restricted Classification*

	Class I-B—Total No., 199	
	Number	Per Cent
Defects of vision	114	57.3
Orthopedic defects	22	11.1
Underdevelopment	20	10.0
Hearing loss	9	4.6
Teeth	7	3.5
Hernia	7	3.5
All other	20	10.0
	Class 4—Total No., 79	
	Number	Per Cent
Defects of vision	39	49.4
Orthopedic defects	9	11.4
Ear defects	8	10.1
Duodenal ulcer	7	8.9
Heart disease	6	7.6
All other	10	12.6

PHYSICAL STRENGTH OR FITNESS TESTS

The physical fitness tests were given by the Department of Physical Education for Men. These tests were designed to give an estimate of the "present condition" of the men relative to their ability to sustain physical effort and to resist fatigue and at the same time to test their native ability for certain types of activities. The tests as given consisted of:

1. The number of times the subject could "push up" on the parallel bars.
2. The number of times he could pull up on the horizontal bar ("chin").
3. The height (in inches) that he could jump (measured from standing reach to jumping reach).
4. The time it took him to run 440 yards.
5. His ability to swim.

The combination of the first three tests of physical fitness has been found to correlate significantly with physical ability and is a relatively good indication of physical development. It is the opinion of the Department of Physical Education and quite generally of the physical education profession that a combination of tests, such as those included in this battery, gives a fairly good indication of the subject's physical condition and ability.

These tests were given to seven hundred and sixty-one university men in the group who were registered for Selective Service. The results of the tests showed that this group of students was approximately 8 per cent below the norm for college men. It seems evident that probably the majority of college men could profit from some program which would "condition" the muscles, thereby making the transition from college life to army service easier for the individual.

SPORTS KNOWLEDGE TEST

A sports knowledge test, which was given to 805 men, consisted of objective tests of ten items on each of fourteen sports. The sports selected were those which are likely to be available to the men who are serving in the various branches of the service. It was the opinion of the Department of Physical Education that a fundamental knowledge of several sports would contribute to the student's ability to use wisely his leisure hours and would therefore be helpful in his adjustment to life in the cantonment. This opinion is based on the fact that, if a person has some knowledge of and skill in an activity, he is more likely to participate in that activity if the opportunity presents itself. Although no norms are available for the tests given, in general it was found that these university men have a fairly adequate knowledge of sports in general but are somewhat lacking in knowledge and skills in individual sports—that is, those sports which require only one or two participants.

HEALTH INFORMATION TESTS

The health information test on personal and public health and hygiene was given to eight hundred and seventeen men in this group. Out of a possible score of 188, the all-college median was 117, with a range from 106 to 146.

When the results of this test were divided according to colleges, it was evident that students in colleges which include health information courses in their curriculums attained the highest scores. The results of this test led us to recommend that all colleges require some course in health education for all students.

On completion of all these tests each student was given a report on his individual results and advised of the facilities which the university had to offer him so that he might make up any deficiencies found.

The information on the number of students who have availed themselves of these facilities on a voluntary basis is not complete, but from the information available it appears that relatively few students have changed their programs to include special work in physical education or personal hygiene. One reason for this is that this plan was started after students had completed registration for the spring quarter and it was difficult for them to make adjustments at that time. It seems evident, however, that if a university is to aid young men in preparing themselves, so far as health and physical fitness are concerned, for army service, a compulsory program must be adopted.

TABLE 2.—*Comparison of Defects*

	University Students Total No., 278	Minnesota Draftees Examined in January 1941 Total No., 2,358
Defects of vision	55.0%*	10.0%*
Orthopedic defects	11.0%	11.0%
Underdevelopment	7.0%	0.5%
Ear defects	8.0%	3.6%
Teeth	3.0%	23.8%
Hernia	2.5%	6.8%
Heart disease	2.2%	9.0%
Tuberculosis	0.0%	1.1%
Venereal diseases	0.0%	1.1%

* Percentage of total defects.

As a result of this trial program in the spring of 1941, the Administrative Committee of the University Senate recommended that, for the fall quarter of the school year 1941-1942,

1. A medical examination be offered again on an optional basis.
2. The faculties of each college of the university consider the desirability of requiring each student to take an introductory course in personal and public health for credit.
3. The physical fitness tests which were given as a part of the spring quarter program be included as a required part of

the medical examination which is compulsory for all incoming students. If this should be done, all students who were found to need "conditioning" could be encouraged to take a carefully planned, individual, remedial program in physical education.

4. In view of the importance of national physical fitness, the colleges of the university institute a required program in physical education with credit.

In addition, a committee has been appointed to prepare for distribution to students and advisers a booklet of information giving systematic guidance and advice on opportunities in courses and activities at the university in the fields of health, physical education and recreation for both selectees and the general student body.

TRAINING OF VOLUNTEER NURSES' AIDES

The U. S. Director of Civilian Defense, Mayor F. H. LaGuardia, announces the training of one hundred thousand volunteer nurses' aides during the next twelve months, in collaboration with the American National Red Cross and the major hospitals of the country. The program is in preparation for a great expansion in hospital beds which may be required during the national emergency.

The growing deficiency in hospital personnel is now being met in part through the training of large numbers of paid subsidiary hospital workers by the NYA, WPA and other agencies. The training program for volunteer nurses' aides is designed to expand the effectiveness of the trained nurse in hospitals, clinics and field nursing services by supplying her with intelligent assistants who can work under her direction.

The curriculum of instruction has been prepared by the Medical Division of the Office of Civilian Defense, the American National Red Cross and the Federal Security Agency. Eligibility is limited to women between the ages of 18 and 50 who have had at least a high school education or its equivalent and who are physically fit. The course will provide eighty hours of intensive instruction in a period of seven weeks. The first half of the course will be given in the local Red Cross chapter house in collaboration with local hospitals and nursing organizations. This will constitute the probationary period and will require two hours of instruction daily on five days a week for four weeks.

The second half of the course will consist of supervised practice in a hospital which has been designated by the Office of Civilian Defense and the Red Cross as a training center. The American National Red Cross will assist the hospital to provide competent instructors and nursing supervisors.

Those who complete the course will be enrolled in the Volunteer Nurses Aide Corps of the American Red Cross with the assurance that they will play an important role in civilian defense. They will retain their membership in the corps only as long as they continue to render adequate service during the period of the national emergency. This is defined as one hundred and fifty hours of volunteer service in a hospital, clinic or field nursing organization in at least one three month period in each calendar year.

The Office of Civilian Defense and the American National Red Cross will provide for this continuing service by arrangement with local hospitals and field nursing agencies. For this purpose the Red Cross will maintain a placement bureau, which will allocate volunteer nurses' aides to the following types of nursing service: hospitals and clinics, visiting nurse (home visiting) agencies, health departments, school health services and industrial hygiene clinics.

By serving in this manner as assistants to qualified nurses, their training will be continued. In the event of sudden emergencies during a period of national crisis they will then be immediately available for reassignment to hospital or field duty by the Office of Civilian Defense. There will be opportunity for some to serve as members of the mobile medical field units which are being organized in hospitals along both seaboards and in industrial centers in the interior, according to plans announced this week by the U. S. Office of Civilian Defense.

Volunteer nurses' aides will wear the uniforms and insignia of civilian defense. The new insignia for nurses' aides will be a red cross within the triangle and circle of the Office of Civilian Defense, indicating that the aide was enrolled and trained by the Red Cross to serve in civilian defense.

Applicants may enroll at the Red Cross chapter house, and the course will begin in each locality as hospital arrangements are completed.

OVERSEAS MEDICAL SUPPLIES ARRIVE SAFELY

The Medical and Surgical Relief Committee of America, 420 Lexington Avenue, New York City, announces in its annual report that supplies valued at $251,698.08 have been shipped overseas during the last year and a half and that every consignment shipped was safely delivered to its destination. While the committee was organized in 1940 to aid Great Britain, the committee has expanded its purpose to provide medical and surgical supplies also for people in China, the Free French, the Free Greeks, the inhabitants of Iceland and the Royal Norwegians on British convoys. The original New York City committee has been augmented by three hundred subcommittees throughout the country and yet the operating expenses have been kept down to 7 per cent of the total receipts, according to Mrs. Rogers Balcom, executive chairman of the committee. Surgical instruments still head the list of requests received from overseas. There is a great demand also for sulfanilamide and its derivatives, for quinine, for vitamins, for tryparsamide and for antitoxins.

RELIEF COMMITTEE SELLS EMBLEMS

The Medical and Surgical Relief Committee of America opened the sale of a new emblem during the annual session of the American Medical Association in June. The emblem has the form of a modified caduceus combined with a sword of mercy and sells for $1. At the ceremony in Cleveland Miss Theodate Johnson, national vice chairman, presented emblems to Drs. Nathan B. Van Etten, New York, then President, and Frank H. Lahey, Boston, now President of the American Medical Association.

During its first year the committee shipped to Great Britain and the allied countries supplies valued at $191,198. The year's operating expenses amounted to 6⅔ per cent of the total receipts, a result attributed to voluntary service on the part of physicians and nurses.

It was announced on June 30 that $10,000 worth of supplies shipped to the Free French in Iceland had arrived safely. Thirteen cases of supplies were recently shipped to relief agencies in Cairo, Egypt.

RESERVE OFFICERS WITH THE SECOND, TENTH AND ELEVENTH INFANTRY

The following medical reserve officers were recently on duty with the regiments indicated in the Sixth Corps Area:

2D INFANTRY

APPELMAN, Howard B., Captain
LEAVITT, Samuel S., 1st Lieut.
MILLARD, Allen L., Major.
NELSON, Charles A., 1st Lieut.
RUBIN, Simon S., Captain.
ROMANSKI, Arthur F., 1st Lieut.
SOROCK, Milton L., 1st Lieut.
SCHUTZMAN, Benjamin M., 1st Lieut.
SINTZEL, Alois R., Captain.
STARSIAK, Casimir R., 1st Lieut.
PEARLMAN, Maurice D., 1st Lieut.
PISZCZEK, Edward A., 1st Lieut.
PRUDOWSKY, Harry, 1st Lieut.
WOOD, Cordelle A., Major.

10TH INFANTRY

BROWNSTEIN, Stanley, 1st Lieut.
DiLORETO, Panfilo C., 1st Lieut.
FEINERMAN, Albert H., 1st Lieut.
NEBINGER, Rankin A., Captain.
STORER, William R., 1st Lieut.
SUGAR, Hyman S., Captain.
THOMAS, Clyde O., Captain.
WILSON, Orley E., 1st Lieut.

11TH INFANTRY

BAUHOF, Ned F., 1st Lieut.
BUERMANN, Henry, Jr., 1st Lieut.
FELDMAN, Emanuel, 1st Lieut.
FLAX, Moses, 1st Lieut.
GREENBERG, Morris Z., 1st Lieut.
KANNER, Irving F., 1st Lieut.
MARCUS, Louis L., 1st Lieut.
RIGHTMAN, Bert, 1st Lieut.
STEIN, Albert F., 1st Lieut.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

SIXTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Sixth Corps Area, which comprises the states of Wisconsin, Michigan and Illinois:

BERNS, Robert S., Captain, Danville, Ill., Headquarters and Station Complement, Corps Area Service Command, Camp Davis, N. C.
DURHAM, Everett William, 1st Lieut., Dearborn, Mich., 202d Corps Area, Fort Bliss, Texas.
FRIEDLAENDER, Sidney, 1st Lieut., Detroit, 33d Division, Camp Forrest, Tenn.
GIBSON, Thomas E., Captain, Lansing, Mich., Station Complement, Selfridge Field, Mich.
HAUSMANN, Richard K., 1st Lieut., Waupun, Wis., 202d Corps Area, Fort Bliss, Texas.
ROSEN, Benjamin B., 1st Lieut., Chicago, 33d Division, Camp Forrest, Tenn.
VEDDER, Charles A., 1st Lieut., Marshfield, Wis., 1604th Corps Area Service Unit, Fort Brady, Mich.
WADE, Chester, 1st Lieut., Chicago U. S. Army Induction Station, Chicago.

Orders Revoked

ANDERSON, E. Gilbert, 1st Lieut., Rockford, Ill.
BRANDEL, John M., 1st Lieut., Owosso, Mich.
CARY, Erwin C., Captain, Reedsville, Wis.
CHRISTIANSON, Oscar O., Captain, Peoria, Ill., 1608th Corps Area Service Unit, Camp Grant, Ill.
DUDEY, Erwin F., Major, Decatur, Ill.
DVORAK, Harold J., Captain, Milwaukee.
ESPEY, Hugh S., 1st Lieut., Chicago.
FELDMAN, Harold, Captain, Pekin, Ill.
GEHRINGER, Norman F., 1st Lieut., Pontiac, Mich.
GOLDSTEIN, Hyman H., 1st Lieut., Chicago, 33d Division, Camp Forrest, Tenn.
HIRSCH, Donald A., 1st Lieut., Chicago.
JACOBS, Maurice B., 1st Lieut., Chicago.
KEHL, Sylvester C., Major, Chicago.
MANTELL, Bernard, 1st Lieut., Maywood, Ill.
MARCUS, Daniel B., 1st Lieut., Detroit.
NELSON, Charles A., 1st Lieut., Pekin, Ill.
O'DONNELL, Steven P., 1st Lieut., Kiel, Wis.
ROBERSON, Brooks L., 1st Lieut., Wood River, Ill.
RUSKIN, Dave B., 1st Lieut., Wahjamega, Mich., 3d Armored Division, Camp Polk, La.
SIMPSON, Reed Morgan, 1st Lieut., Medora, Ill.
VERMEREN, Paul C., 1st Lieut., Chicago.

SEVENTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Seventh Corps Area, which comprises the states of North Dakota, South Dakota, Minnesota, Nebraska, Iowa, Kansas, Missouri, Arkansas and Wyoming:

AHERN, Gerald Steber, 1st Lieut., Minneapolis, 6th Medical Battalion, Fort Leonard Wood, Mo.
AHRENS, John Heideman, 1st Lieut., University City, Mo., Corps Area Service Command, Replacement Center Infirmary, Fort Leonard Wood, Mo.
ANDERSON, Wallace Everett, 1st Lieut., Thief River Falls, Minn., Camp Grant, Ill.
ANNEBERG, Paul Daniel, 1st Lieut., Carroll, Iowa, Corps Area Service Command Engineers Replacement Center Infirmary, Fort Leonard Wood, Mo.
ANSCHUETZ, Robert Ralph, 1st Lieut., Kansas City, Mo., Camp Grant, Ill.
AYLWARD, Howard Joseph, 1st Lieut., Clayton, Mo., Corps Area Service Command Station Hospital, Camp J. T. Robinson, Ark.
BACA, Donaciano E., 1st Lieut., Papillion, Neb., Corps Area Service Command Station Hospital, Fort Riley, Kan.
BARKER, John Dennis, 1st Lieut., Warren, Minn., Air Base, Portland, Ore.
BARKER, Lawrence Fergusson, 1st Lieut., St. Louis, 1st Field Artillery Battalion, Fort Leonard Wood, Mo.
BARRENT, Milton Edward, 1st Lieut., Sioux City, Iowa, Camp Grant, Ill.
BARRY, William Burnett, 1st Lieut., Kansas City, Mo., Corps Area Service Command, Station Hospital, Fort F. E. Warren, Wyo.
BECHTOLD, Frederick Frank, 1st Lieut., St. Louis, Corps Area Service Command Replacement Center Infirmary, Jefferson Barracks, Mo.
BISHOP, Marion Dale, 1st Lieut., St. Louis, Camp Grant, Ill.
BLAIR, James Berl, 1st Lieut., Broken Bow, Neb., Corps Area Service Command, Engineer Replacement Center Infirmary, Fort Leonard Wood, Mo.
BOYD, Eugene Judd, 1st Lieut., Iowa City, Corps Area Service Command Station Hospital, Fort Riley, Kan.
BRADLEY, Ben Hughes, 1st Lieut., Richmond Heights, Mo., 20th Infantry, Fort Leonard Wood, Mo.
BUELL, Arthur Louis, 1st Lieut., Batesville, Ark., Replacement Training Center, Camp Grant, Ill.
BUSSABARGER, Robert Allison, 1st Lieut., Wardell, Mo., 43d Engineers, Camp J. T. Robinson, Ark.
CAMPBELL, Harry Bryant, 1st Lieut., St. Louis, 20th Infantry, Fort Leonard Wood, Mo.
CAMPBELL, Robert Evans, Jr., 1st Lieut., Cedar Rapids, Iowa, Corps Area Service Command Induction Station, Fort Des Moines, Iowa.
CARLSON, Elmer Henry, 1st Lieut., Muscatine, Iowa, Fort Leonard Wood, Mo.
CARP, Oscar, 1st Lieut., Omaha, Corps Area Service Command Reception Center Infirmary, Camp J. T. Robinson, Ark.
CASEY, Elmer Barney M., Lieut. Colonel, St. Louis, Camp Grant, Ill.
CONTI, James Philip, 1st Lieut., St. Louis, 20th Infantry, Fort Leonard Wood, Mo.
COUCH, Orrie Alexander, Jr., 1st Lieut., Iowa City, Iowa, Camp Grant, Ill.
CURTIS, William Shepley, 1st Lieut., St. Louis, Camp Grant, Ill.
DAVIS, Christopher Gates, 1st Lieut., Kansas City, Kan., Camp Grant, Ill.
DEW, Hogan Allen, 1st Lieut., Hamburg, Ark., 1st Infantry, Fort Leonard Wood, Mo.
DONNELLY, Bernard Aloysius, 1st Lieut., Iowa City, Fort Douglas, Utah.
DORMAN, John Wesley, 1st Lieut., Dyess, Ark., 142d Field Artillery, Fort Sill, Okla.
DRACE, Charles Centennial, Jr., 1st Lieut., St. Louis, McChord Field, Tacoma, Wash.
DREXLER, George Warren, 1st Lieut., Minneapolis, 1st Infantry, Fort Leonard Wood, Mo.
DUPONT, Joseph Arthur, 1st Lieut., Excelsior, Minn., 6th Medical Battalion, Fort Leonard Wood, Mo.
ELLIOTT, William Henry, Jr., 1st Lieut., St. Louis, Corps Area Service Command Station Hospital, Fort Meade, S. D.
EVANS, Byron Henry, 1st Lieut., Cedar Rapids, Iowa, Camp Grant, Ill.
FERGUSON, Lewis Hamilton, 1st Lieut., St. Louis, Camp Grant, Ill.
FLYNN, John Timothy, 1st Lieut., St. Louis, Fort Leonard Wood, Mo.
FOSTER, Miles Everett, 1st Lieut., St. Louis, Fort Leonard Wood, Mo.
GALT, Charles E., Jr., 1st Lieut., Ferguson, Mo., Camp Grant, Ill.
GARETZ, Michael Allen, 1st Lieut., Minneapolis, 6th Medical Battalion, Fort Leonard Wood, Mo.
GARRETT, Glenn Harley, 1st Lieut., Clay Center, Kan., for temporary duty with Medical Replacement Training Center, Camp Grant, Ill.
GATES, Charles Lee, 1st Lieut., Urich, Mo., Corps Area Service Command Station Hospital, Fort Leavenworth, Kan.
GEPPERT, Leo Joseph, 1st Lieut., Vermillion, S. D., Camp Grant, Ill.
GERSON, Charles Everett, 1st Lieut., St. Louis, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
GLASSMAN, Arthur Leonard, 1st Lieut., Iowa City, Engineers Replacement Center Infirmary, Fort Leonard Wood, Mo.
GRAVES, James Huntington, 1st Lieut., St. Paul, 92d Engineer Battalion, Fort Leonard Wood, Mo.
GRAY, Herschel Fredrick, 1st Lieut., Little Rock, Ark., 1st Infantry, Fort Leonard Wood, Mo.
GREENHOUSE, Jerome Mayer, 1st Lieut., University City, Mo., Camp Grant, Ill.
GREGORY, Kendall Decatur, 1st Lieut., St. Louis, Camp Grant, Ill.
HAMILTON, Charles Ferrill, 1st Lieut., Iowa City, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
HAMILTON, Ralph Block, Ist Lieut., West Memphis, Ark., Air Base (Nonflying status), Everett, Wash.
HARPER, Harry Penn, 1st Lieut., Rochester, Minn., Corps Area Service Command Station Hospital, Fort Riley, Kan.
HARRIS, Charles Preston, 1st Lieut., Leachville, Ark., Air Base (Nonflying status), Pendleton, Ore.
HAWES, William John, Major, Columbia, Mo., Headquarters and Headquarters Battery, 6th Division Artillery, Fort Leonard Wood, Mo.
HAZLET, Kenneth Kirk, Iowa City, Corps Area Service Command, Station Hospital, Fort Leonard Wood, Mo.
HEIMANN, Verne Rodney C., 1st Lieut., Albia, Iowa, Corps Area Service Command Induction Station, Fort Snelling, Minn.
HEITZMAN, Paul Otto, 1st Lieut., Burlington, Iowa, 51st Field Artillery Battalion, Fort Leonard Wood, Mo.
HENDERSON, Walker Bland, Major, Oelwein, Iowa, 6th Medical Battalion, Fort Leonard Wood,, Mo.
HEYWOOD, Leo Thomas, 1st Lieut., Omaha, Fort Leonard Wood, Mo.
HILGER, David William, 1st Lieut., St. Paul, Corps Area Service Command Induction Station, Fort Leavenworth, Kan.
HOBART, Francis William, Captain, Lake City, Iowa, Medical Replacement Center, Camp Grant, Ill.

HOGABOOM, Gilbert Murray, 1st Lieut., Hot Springs, Ark., 35th Division, Camp Joseph T. Robinson, Ark.
HOFFMAN, George Robert, 1st Lieut., Minneapolis, 1st Infantry, Fort Leonard Wood, Mo.
HOLLENHORST, Robert William, 1st Lieut., St. Cloud, Minn., 6th Medical Battalion, Fort Leonard Wood, Mo.
HOPKINS, Florian Goss, 1st Lieut., Gideon, Mo., Corps Area Service Command Station Hospital, Camp J. T. Robinson, Ark.
HOTTINGER, Raymond Creighton, 1st Lieut., Jamesville, Minn., Fort George Wright, Spokane, Wash.
HOWE, Louis Francis, Captain, Union, Mo., Medical Replacement Center, Camp Grant, Ill.
HUBER, Tyron Ehrhart, 1st Lieut., St. Louis, Camp Grant, Ill.
HURST, Thomas Charles, 1st Lieut., Kansas City, Mo., Camp Grant, Ill.
JANUARY, Lewis Edward, 1st Lieut., Iowa City, Corps Area Service Command Quartermaster Replacement Center Infirmary, Fort F. E. Warren, Wyo.
JOHNSON, Robert Hall, 1st Lieut., St. Louis, 6th Medical Battalion, Fort Leonard Wood, Mo.
JORDAN, Raymond Ellsworth, 1st Lieut., St. Louis, Medical Replacement Training Center, Camp Grant, Ill.
KAISER, Max Elliott, 1st Lieut., Ottawa, Kan., Medical Replacement Center, Camp Grant, Ill.
KEOHEN, Gerald Francis, 1st Lieut., Iowa City, Iowa, Camp Grant, Ill.
KILTZ, Richard Clyde, Captain, Omaha, Corps Area Service Command Induction Station, Fort Cook, Neb.
KIMBALL, John Egbert, Jr., 1st Lieut., St. Louis, Camp Grant, Ill.
KINGSLAND, Robert Chenault, 1st Lieut., St. Louis, Corps Area Service Command Station Hospital, Fort Crook, Neb.
KLAFF, Daniel David, 1st Lieut., St. Louis, for temporary duty with Medical Replacement Training Center, Camp Grant, Ill.
KNIGHT, William Allen, Jr., 1st Lieut., St. Louis, Camp Grant, Ill.
KOBER, William Melvin, 1st Lieut., Little Rock, Ark., 4th Cavalry, Fort Meade, S. D.
KOTNER, Lawrence Melvin, 1st Lieut., University City, Mo., Quartermaster Replacement Center Infirmary, Fort F. E. Warren, Wyo.
KRAVITZ, Morton Atherton, 1st Lieut., Kansas City, Corps Area Service Command Station Hospital, Fort Riley, Kan.
KUGLER, Frank Elbert, 1st Lieut., Iowa City, Corps Area Service Command Station Hospital, Fort F. E. Warren, Wyo.
KURIS, David B., 1st Lieut., Duluth, Minn., 6th Medical Battalion, Fort Leonard Wood, Mo.
LAKAYTIS, Charles Alexandra, 1st Lieut., Kansas City, Mo., Camp Grant, Ill.
LATTUADA, Henry Deter, 1st Lieut., St. Louis, Replacement Training Center, Camp Grant, Ill.
LAUDICINA, August, 1st Lieut., St. Louis, Corps Area Service Command, Station Hospital, Fort Snelling, Minn.
LEE, Wayne Robert, 1st Lieut., Burlington, Iowa, Corps Area Service Command Quartermaster Replacement Center Infirmary, Fort F. E. Warren, Wyo.
LIMAURO, Andrew Benedict, 1st Lieut., St. Louis, Camp Grant, Ill.
LINDLEY, Ellsworth LaVerne, 1st Lieut., Muscatine, Iowa, 1st Infantry, Fort Leonard Wood, Mo.
LONDON, Lewis Bolter, 1st Lieut., Little Rock, Ark., Corps Area Service Command Station Hospital, Camp J. T. Robinson, Ark.
LONERGAN, Warren Mellies, 1st Lieut., St. Louis, Camp Grant, Ill.
LOVE, William Robert, 1st Lieut., Rochester, Minn., Corps Area Service Command Station Hospital, Fort Snelling, Minn.
MacDONALD, William Charles, 1st Lieut., St. Louis, Camp Grant, Ill.
McCAIN, Donovan Legare, 1st Lieut., St. Paul, Corps Area Service Command Station Hospital, Fort F. E. Warren, Wyo.
McCONKIE, Edwin Bruce, Captain, Cedar Rapids, Iowa, Corps Area Service Command Replacement Center Infirmary, Jefferson Barracks, Mo.
McDONALD, George James, 1st Lieut., St. Louis, Corps Area Service Command Station Hospital, Fort Snelling, Minn.
McGROARTY, Brian John, 1st Lieut., Easton, Minn., Camp Grant, Ill.
McKEE, Leo Francis, 1st Lieut., Kansas City, Kan., Corps Area Service Command, Replacement Center Infirmary, Fort Leonard Wood, Mo.
MACKENBROCH, Frederick Caspar, 1st Lieut., Omaha, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
MADDUX, William Paul, 1st Lieut., Buffalo, Mo., Quartermaster Replacement Center Infirmary, Fort F. E. Warren, Wyo.
MARK, Hilbert, Major, Minneapolis, Camp Grant, Ill.
MARKING, George Henry, 1st Lieut., Osseo, Minn., Camp Grant, Ill.
MELLIES, Chester John, Captain, Mount Vernon, Mo., Corps Area Service Command Station Hospital, Fort Riley, Kan.
MERENDA, Sam John, 1st Lieut., St. Louis, 6th Division Headquarters and Headquarters Battery, Fort Leonard Wood, Mo.
MERRILL, Robert Lowe, 1st Lieut., St. Louis, Camp Grant, Ill.
MINGE, Raymond Kenneth, 1st Lieut., Clarkfield, Minn., 92d Engineer Battalion, Fort Leonard Wood, Mo.
MIRA, Joseph John, 1st Lieut., St. Louis, Camp Grant, Ill.
MOEN, Berwyn Harold, 1st Lieut., Inwood, Iowa, Camp Grant, Ill.
MORGAN, John Lloyd, 1st Lieut., Emporia, Kan., Camp Grant, Ill.
MULLER, Albrecht Eugene, 1st Lieut., St. Paul, 6th Medical Battalion, Fort Leonard Wood, Mo.
MUNDT, Leslie Krow, 1st Lieut., Helena, Ark., Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
MUNSCH, Girard Augustus, 1st Lieut., St. Louis, Camp Grant, Ill.
MURRAY, Edward Stevenson, 1st Lieut., Cedar Rapids, Iowa, Corps Area Service Command Quartermaster Replacement Center Infirmary, Fort F. E. Warren, Wyo.
NESTER, Charles Adolph, 1st Lieut., St. Louis, Camp Grant, Ill.
NEURNBERGER, Robert Earl, 1st Lieut., Omaha, 80th Field Artillery Battalion, Fort Leonard Wood, Mo.
NOTHNAGEL, Arnold Fred, 1st Lieut., Kansas City, Kan., Corps Area Service Command Station Hospital, Fort Riley, Kan.
OGBORN, Robert James, 1st Lieut., Sioux Falls, S. D., 6th Medical Battalion, Fort Leonard Wood, Mo.
OLSON, Alton Curtis, 1st Lieut., Minneapolis, Corps Area Service Command Station Hospital, Fort Riley, Kan.
OLSON, Duane Charles, 1st Lieut., Gaylord, Minn., Camp Grant, Ill.
QUATTLEBAUM, Frank Walter, 1st Lieut., Crookston, Minn., Camp Grant, Ill.
PANGBURN, Merrill Walter, 1st Lieut., Miller, S. D., nonflying status, Moffett Field, Calif.
PASSANANTE, Bartholomew M., 1st Lieut., University City, Mo., 63d Infantry, Fort Leonard Wood, Mo.
PAYNE, Voris Ralph, 1st Lieut., St. Louis, Camp Grant, Ill.
PETTERSON, Cecil Edward, 1st Lieut., Norton, Kan., Ogden Air Depot (nonflying status), Ogden, Utah.
POHLMAN, John Francis, 1st Lieut., Wichita, Kan., Camp Grant, Ill.
RICH, George Theodore, 1st Lieut., Grand Forks, N. D., Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
REEVES, Eugene Albert, 1st Lieut., Kansas City, Kan., Camp Grant, Ill.
REID, Joe Winston, 1st Lieut., Arkadelphia, Ark., Camp Grant, Ill.
RITTER, Eugene Francis, 1st Lieut., Coatesville, Mo., 6th Engineer Battalion, Fort Leonard Wood, Mo.
ROBERTSON, Howard Thomas, 1st Lieut., Concordia, Kan., Camp Grant, Ill.
RODMAN, George Hurst, 1st Lieut., St. Louis, Camp Grant, Ill.
SAAR, John William, 1st Lieut., Salt Lake City, Ogden Air Depot (nonflying status), Ogden, Utah.
SCALES, James Russell, 1st Lieut., Rochester, Minn., 6th Engineer Battalion, Fort Leonard Wood, Mo.

Orders Revoked

AAGESEN, Carl A., 1st Lieut., Dows, Iowa.
AYLWARD, Howard Joseph, 1st Lieut., Clayton, Mo., 6th Division, Headquarters and Headquarters Battery, Fort Leonard Wood, Mo.
BAILEY, William H., 1st Lieut., St. Louis.
BEBER, Meyer, Captain, Omaha.
BERMAN, William, 1st Lieut., St. Louis.
BIRGE, Richard Fuller, Captain, Des Moines, Iowa, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
BLAIR, James Berl, 1st Lieut., Broken Bow, Neb.
BOE, Henry, Captain, Sioux City, Iowa.
BOLEY, James O., 1st Lieut., Pilot Grove, Mo.
BURT, Elmer G., 1st Lieut., Crossett, Ark.
BUZZELLE, Leonard K., 1st Lieut., Minneapolis.
CAIRNS, Robert J., 1st Lieut., Sanborn, Minn.
DECKER, Rudolph F., Captain, Byron, Neb.
DRACE, Charles Centennial, Jr., 1st Lieut., St. Louis.
DREXLER, George Warren, 1st Lieut., Minneapolis.
EDWARDS, Thomas Jefferson, 1st Lieut., St. Paul, Corps Area Service Command Station Hospital, Fort Leonard Wood, Mo.
ENGLISH, Wallace D., Captain, Cardwell, Mo.
ERICKSON, Clarence Wilber, 1st Lieut., Pittsburg, Kansas, Corps Area Service Command Station Hospital, Fort Crook, Neb.
FAST, William S., 1st Lieut., Atchison, Kan.
FLICKINGER, Roger R., 1st Lieut., Mason City, Iowa.
FLYNN, John Timothy, 1st Lieut., St. Louis, Corps Area Service Station Hospital, Fort Leonard Wood, Mo.
GRAY, Herschel Fredrick, 1st Lieut., Little Rock, Ark., 1st Infantry, Fort Leonard Wood, Mo.
HAGAN, Francis J., 1st Lieut., Wichita, Kan.
HAMILTON, Benjamin C., Jr., Major, Jefferson, Iowa.
HAYMOND, Harold E., Captain, Perry, Iowa.
HENDERSON, Robert W., Captain, Bismarck, N. D.
HOBART, Francis William, Captain, Lake City, Iowa.
HOBBS, Russell E., 1st Lieut., Wichita, Kan.
HOFFMAN, Jacob S., 1st Lieut., Kansas City, Mo.
HOWE, Louis Francis, Captain, Union, Mo., Medical Department Replacement Center, Camp Grant, Ill.
HUBER, Melvin J., Captain, St. Louis.
HUGHES, Shelby B., 1st Lieut., Clinton, Mo.
HYNDMAN, Henry H., 1st Lieut., Wichita, Kan.
JEWELL, Iverson H., Lieut., Colonel, Paris, Ark.
JOHNSTON, Thomas S., Captain, Topeka, Kan.
LEIFER, William W., 1st Lieut., Kansas City, Mo.
McVAY, Melvin J., Captain, Lake City, Iowa.
MADDUX, William Paul, 1st Lieut., Buffalo, Mo.
MINER, Paul Floyd, 1st Lieut., Laramie, Wyo., 35th Division, Camp J. T. Robinson, Ark.
MINGE, Raymond Kenneth, 1st Lieut., Clarkfield, Minn.
PLATOU, Ralph V., 1st Lieut., Minneapolis.
POTASHNICK, Robert, 1st Lieut., St. Louis, Camp Roberts, Calif.
REED, Charles C., 1st Lieut., Little Rock, Ark.
SETTLE, Emmett B., Captain, Rockport, Me.
SHANDORF, James F., 1st Lieut., Northfield, Minn.
SHELTON, Harold J., Captain, Webster Groves, Mo.
SHEPEARD, Walter Lee, 1st Lieut., Pittsburg, Kan.
SICELUFF, Joseph G., 1st Lieut., Springfield, Mo.
SPAFFORD, Allen L., Captain, Osawatomie, Kan.
STEELE, Hugh H., 1st Lieut., Deadwood, S. D.
TROW, James Edward, 1st Lieut., Minneapolis.
VAN BESIEN, George J., 1st Lieut., Decorah, Iowa.
WETRICH, Max Franklin, 1st Lieut., Des Moines, Iowa, 63d Infantry, Fort Leonard Wood, Mo.

ORGANIZATION SECTION

WOMAN'S AUXILIARY

Death of Mrs. Red

Mrs. Samuel Clark Red of Houston, Texas, founder of the Woman's Auxiliary to the American Medical Association, died suddenly on August 10. Mrs. Red was the first president of the Auxiliary to the American Medical Association (1922-1923) and was also president for the two succeeding years.

Arkansas

On March 13 Mrs. James Lewis, retiring president of the auxiliary to the Washington County Medical Society, was hostess to members at a dinner bridge; officers for next year were elected as follows: president, Mrs. E. F. Ellis, Fayetteville; vice president, Mrs. R. T. Henry, Springdale; secretary, Mrs. P. L. Hathcock Jr.; treasurer, Mrs. R. H. Huntington. On March 20 the annual City Hospital Shower and Tea was given by the auxiliary. About 100 guests were present and six hundred gifts for the hospital were received. Mrs. Fount Richardson was general chairman of the tea. On March 24 Mrs. James Lewis read a paper before the Business and Professional Woman's Club of Fayetteville at the showing of the picture "Choose to Live," sponsored by the Woman's Auxiliary to the American Medical Association. On March 25 the auxiliary sponsored the same picture with the P. T. A. at the high school auditorium, to which the public is invited.

California

On April 15 the Sacramento auxiliary sponsored a fashion show for juveniles, the models being twenty daughters and sons of the group.

One hundred thirty-three members and guests of the Los Angeles County auxiliary met at the Annandale Golf Club in Pasadena to hear Mrs. Thomas G. Winter of the Motion Picture Producers and Distributers of America talk on "The Pictures and the Political Crisis."

Colorado

The auxiliary to the Denver County Medical Society met April 21 at the Colorado General Hospital nurses' home to hear a dramatization by Jeanette Humphreys of the play entitled "George Washington Slept Here." The members brought their banks for the benefit of cancer control.

Indiana

Dr. Doster Buckner addressed the Allen County medical auxiliary March 18 in Fort Wayne on "Danger in Laity Discussion of Scientific Information." Dr. Jessie Calvin, vice commander in the Woman's Field Army for Cancer Control, talked on "Cancer Control," and Mrs. A. N. Ferguson discussed "The Case of the United States vs. The American Medical Association et al." The auxiliary has arranged to distribute toys in the pediatric wards of Fort Wayne hospitals.

Seventeen members attended the dinner meeting of the auxiliary to the Delaware-Blackford Counties Medical Society in Muncie on March 18. The group recently gave the physicians $40 to purchase a dictionary for the physicians' library in the Ball Memorial Hospital.

The members from Nappanee planned the program for the meeting on March 6 of the Elkhart County auxiliary. Mrs. Howard A. Bosler, whose husband has been a physician in Nigeria, West Africa, described her experiences as a doctor's wife there. On March 20 the Elkhart County Medical Society was addressed by Dr. Bosler, who gave an account of his work in Nigeria.

The LaPorte County auxiliary held a dinner meeting in Michigan City on March 20. Following the dinner, the discussion of socialized medicine was led by a member of the Michigan City League of Women Voters.

The Madison County auxiliary is proud of the success of its program in which it sponsored a drawing for a prize of $300 or a trip to Mexico or California, the winner to make his own choice. The funds raised in this way were used for guild purchases of various supplies and equipment for St. John's Hospital.

The Tippecanoe County auxiliary has been experimenting; at each meeting it has a "news flash" of up to the minute news pertaining directly or indirectly to the medical world. This tends to encourage the members to watch for news items to report and is a step toward an informed public. The auxiliary is confining its programs to ones of an educational nature and letting the social part be secondary.

Iowa

The Woman's Auxiliary to the Upper Des Moines Medical Society met at Spirit Lake, July 10. Mrs. W. R. Hornaday of Des Moines, president of the auxiliary to the Iowa State Medical Society, stressed the aims and purposes of the auxiliary, which she cited as being (1) social, (2) a means of contact between the medical profession and laymen and (3) the necessity of having at least one health program annually in each auxiliary. The following officers were elected for the coming year: Mrs. Don F. Rodawig of Spirit Lake, president; Mrs. Paul O. Nelson of Emmetsburg, vice president; Mrs. Andrew I. Reed of Estherville, secretary and treasurer, and Mrs. Elbert E. Munger Jr. of Spencer, ex-committee member from Clay County.

The Woman's Auxiliary to the Dubuque County Medical Society held its annual meeting April 8. Mrs. E. T. Warren, president of the state auxiliary, was guest of honor. Miss Janice Bardill played piano selections.

Wives of physicians met with Mrs. E. T. Warren of Stuart, president of the state auxiliary, April 3 in Jefferson and organized the Woman's Auxiliary to the Greene County Medical Society. The following officers were elected: Mrs. Phillips E. Lohr of Churdan, president; Mrs. Roy E. Parry of Scranton, president-elect; Mrs. Walter E. Chase of Rippey, secretary and treasurer, and Mrs. Laurence C. Hanson of Jefferson, chairman of the Hygeia committee.

North Carolina

The nineteenth session of the Woman's Auxiliary to the Medical Society of the State of North Carolina was held at Pinehurst, Tuesday, May 20. Mrs. Clyde R. Hedrick of Lenoir, president, presided. Dr. Hubert B. Haywood, president of the Medical Society of the State of North Carolina, was guest speaker. The chairman of the committee on research, Mrs. R. S. McGeachy of New Bern, gave a paper on the life of the late Dr. Martin L. Stevens, for whom the bed which the woman's auxiliary will support at Black Mountain Sanatorium is named. The report of the nomination committee was as follows: Mrs. Sidney Smith, Raleigh, president; Mrs. R. A. Moore, Winston-Salem, president-elect; Mrs. C. R. Hedrick, Lenoir, first vice president; Mrs. J. R. Terry, Lexington, second vice president; Mrs. J. S. Hooker, Chapel Hill, third vice president; Mrs. Harry Winkler, Charlotte, corresponding secretary and recording secretary, and Mrs. E. C. Judd, Raleigh, treasurer.

Pennsylvania

The auxiliary of the Westmoreland County Medical Society was addressed May 6 by Dr. W. W. Bauer of Chicago, director of the Bureau of Health Education of the American Medical Association on "The Skin You Love to Retouch." Dr. Bauer had addressed high school students in the morning and the Rotary Club at noon. The auxiliary has given thirty-eight subscriptions of *Hygeia* to schools and libraries in the county during the past year. Miss Ann Carlisle played during the tea; high school girls were aides, Mrs. R. E. L. McCormick of Irwin was chairman of the tea arrangements and Mrs. J. Morgan Meyhew of Greensburg had charge of the program.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Changes in Health Personnel.—Dr. William A. Dodson Jr., Double Springs, has resigned as health officer of Winston County to take a position with the U. S. Public Health Service, it is reported.——Dr. William J. Donald, Brewton, has been appointed an associate in county organization in the state department of health, Montgomery, to succeed Dr. W. D. Burkhalter, who recently became health officer of Shelby County of Memphis, Tenn.——Dewitt Sterling Abell, M.S., a member of the staff of the North Carolina State Department of Health, has been appointed director of the bureau of sanitation in the Alabama State Health Department.

ARKANSAS

Medical Alumni Officers.—Dr. Eugene A. Callahan, Carlisle, was elected president of the Alumni Association of the University of Arkansas School of Medicine; Dr. Estes Allen, Little Rock, vice president; Dr. Thomas Duel Brown, secretary, and Dr. Paul M. Fulmer, Little Rock, treasurer.

District Meeting.—The Ninth Councilor District Medical Society met at the Hotel Seville, Harrison, recently, with the following speakers:

Dr. Arthur M. Washburn, Little Rock, Tularemia.
Dr. Le Roy F. Heimburger, Springfield, Mo., Fungi in Eczematous Dermatitis of the Hands.
Dr. Walter S. Sewell, Springfield, Mo., Diseases of the Prostate.
Dr. Charles S. Paddock, Fayetteville, Urologic Problems That Daily Confront the Physician.
Dr. Louis K. Hundley, Harrison, Trachoma in Arkansas.

Society News.—The Mississippi County Medical Society was addressed recently by Drs. Robert Lyle Motley and Thomas D. Moore, Memphis, on "Indigestion" and "Ureteral Kinks and Strictures" respectively.——Dr. James T. Powell, Gravette, discussed podalic version and solution of posterior pituitary before the Benton County Medical Society, June 12, at Gravette.——A joint dinner session of the Sebastian County Medical Society and the Muskogee County (Okla.) Medical Society, June 10, in Fort Smith was addressed by Drs. Henry T. Ballantine, Muskogee, on "Anomalies of the Newborn" and Frederic G. Dorwart, Muskogee, "Massive Collapse of the Lung and Pneumothorax."——Drs. Francis Walter Carruthers and Paul L. Mahoney, Little Rock, addressed the Southeast Arkansas Medical Society in Crossett, June 16, on "Synovectomy in Knee Joint Conditions" and "Chronic Cough" respectively. Dr. Herbert Fay H. Jones, Little Rock, president of the Arkansas Medical Society, also made an address.——Dr. Willard W. M. Allen, St. Louis, addressed the Pulaski County Medical Society, June 23, on "Clinical Use of Sex Hormones."

FLORIDA

Annual Postgraduate Course.—The Florida Medical Association and the Florida State Board of Health sponsored their ninth annual short course for physicians in Jacksonville in June. Speakers who gave several lectures each were:

Medicine, Dr. Henry M. Thomas Jr., Baltimore.
Surgery, Dr. Richard B. Cattell, Boston.
Obstetrics, Dr. Nicholson J. Eastman, Baltimore.
Pediatrics, Dr. Daniel C. Darrow, New Haven, Conn.
Gynecology, Dr. Everett D. Plass, Iowa City.
Venereal diseases, Dr. Charles F. Mohr, Baltimore.
Military Medicine, Col. Luther R. Poust, Lieut. Col. Bennett G. Owens, Major James A. Coleman, all of Camp Blanding, and Comdr. Eben E. Smith, Naval Air Station, Jacksonville.

GEORGIA

Memorial to Dr. E. C. Davis.—Plans to establish a memorial for the late Dr. Edward Campbell Davis in the new Academy Building, home of the Fulton County Medical Society, Atlanta, have been announced. Dr. Davis died in 1931. A graduate of the University of Louisville School of Medicine in 1892, Dr. Davis was emeritus professor of obstetrics and gynecology at Emory University School of Medicine, a founder of the Davis-Fischer Sanatorium and, in 1928, president of the Fulton County Medical Society.

ILLINOIS

Family Health Consultations at State Fair.—Family health consultations were a feature of the state fair exhibits of the Illinois State Department of Public Health at the Exposition Building in Springfield, August 9-17. This feature supplanted the discontinued baby conference and consisted of consultation booths open to adults, infants and children of all ages. Trained specialists in public health engineering, nursing, sanitation, preventive medicine, mental hygiene and nutrition were on hand to discuss general health problems with visitors at the fair.

Chicago

Personal.—Dr. Samuel M. Feinberg has been elected an honorary member of the Argentine Society for the Study of Allergy.——Mr. Charles A. Wordell, director of St. Luke's Hospital for thirteen years, has resigned to become superintendent of the Hospital for Children, San Francisco, effective September 1.

Dr. McNally Appointed Toxicologist.—Dr. William D. McNally, who is said to have been responsible for the establishment of the first laboratory for toxicology in the nation for the Cook County coroner's office in 1913, has again been appointed toxicologist for the county, effective August 11. He succeeds Clarence W. Muehlberger, Ph.D., who has become toxicologist for the state of Michigan. Dr. McNally served as toxicologist and chief chemist of Cook County from 1913 to 1929. He was instructor in chemistry at the University of Illinois from 1905 to 1906, when he went to Armour & Company as chemist. He was chief chemist of the Chicago Department of Health from 1910 to 1913. Since 1923 he has been associate professor of materia medica and toxicology at Rush Medical College. He graduated at Rush in 1920. Dr. Muehlberger had been county toxicologist since 1930. He came from Wisconsin, where he had been state toxicologist since 1923 and assistant professor of pharmacology and toxicology at the University of Wisconsin Medical School, Madison, since 1924. Dr. Muehlberger was toxicologist and assistant director of the Scientific Crime Detection Laboratory at Northwestern University Medical School, 1930-1935 and had held teaching positions at Northwestern, Illinois and the University of Chicago, Department of Medicine.

MASSACHUSETTS

Dr. Beecher Lectures in Bogotá.—The U. S. Department of State awarded a travel grant to Dr. Henry K. Beecher, associate in anesthesia, Harvard Medical School, Boston, to give a series of lectures during June and July at the National University of Colombia at Bogotá, *Science* reports.

Promotions on Harvard Faculty.—The following promotions on the faculty of Harvard Medical School, Boston, were recently announced, among others:

Donald L. Augustine, Sc.D., associate professor of comparative pathology and tropical medicine.
Dr. William L. Aycock, associate professor of preventive medicine and hygiene.
Dr. Harry C. Solomon, clinical professor of psychiatry.
Dr. Charles G. Mixter, clinical professor of surgery.
Dr. Robert S. Morison, assistant professor of anatomy.
Dr. Thomas D. Jones, assistant professor of medicine.
Dr. Aubrey O. Hampton, assistant professor of roentgenology.
Dr. Arthur T. Hertig, assistant professor of pathology.
Dr. Jacob Fine, assistant professor of surgery.
Dr. Harold G. Tobey, lecturer on laryngology.
Dr. Charles T. Porter, lecturer on otology.
Dr. George G. Smith, lecturer in genitourinary surgery.

MICHIGAN

New Health Units.—A new city-county health unit has been established in Kalamazoo County under the direction of Dr. Irmel W. Brown, formerly health officer of Kalamazoo, who has returned from a year's study in public health. This is the first city-county unit in Michigan. There are now sixty-five counties in the state with full time public health services and eighteen counties without such protection.

Dr. Francis Named Professor of Epidemiology.—Dr. Thomas Francis Jr., professor of bacteriology and director of the bacteriologic laboratories, New York University College of Medicine, New York, has been appointed professor and head of the department of epidemiology at the new School of Public Health at the University of Michigan, Ann Arbor. Dr. Francis was born in Indiana in 1899. He graduated at Yale University School of Medicine, New Haven, in 1925. He was at one time resident physician at the Hospital of the Rockefeller Institute and associate in medicine at the Rockefeller Institute. He has been a member of the staff of the International Health Division of the Rockefeller Foundation since 1936.

MISSOURI

Dr. Myers Honored.—The Kansas City Society of Ophthalmology and Otolaryngology at a recent meeting presented a gold medal to Dr. John L. Myers, Kansas City, as a mark of appreciation of his work in the society. Dr. Myers was president of the society in 1921 and of the Kansas City Southwest Clinical Society in 1931. Since 1926 he has been secretary for otolaryngology of the American Academy of Ophthalmology and Otolaryngology. Dr. Myers took his medical degree at the College of Physicians and Surgeons, now the University of Kansas School of Medicine, Kansas City, Kan., in 1904 and has been associate professor of otolaryngology at the school since 1926. He has practiced in Kansas City (Mo.) since 1916.

New Professor of Clinical Medicine. — Dr. Harry L. Alexander, associate professor of clinical medicine at Washington University School of Medicine, St. Louis, has been appointed professor of clinical medicine and acting head of the department of internal medicine. He succeeds Dr. David P. Barr, who resigned to accept an appointment at Cornell University Medical College, New York. Dr. Alexander was born in New York in 1887. He graduated at Columbia University College of Physicians and Surgeons in 1914. He was associate professor of medicine at Washington from 1924 to 1936, when he became associate professor of clinical medicine. He has been president of the Society for the Study of Asthma and Allied Conditions and of the Association for the Study of Allergy. He served with the American Expeditionary Forces, 1918-1919, and, with the title of major, medical corps, was physician in chief of Camp Hospital number 52, Le Mans, France.

NEW JERSEY

Activities of State Medical Board.—The state board of medical examiners has reported the following actions, among others, against illegal practitioners:

Frank Bangham, Jersey City, a registered pharmacist, paid the penalty for practicing medicine without a license.

West A. Durfor, Haddon Heights, an unlicensed chiropractor, paid a penalty for practicing without a license.

John D. McManamy, Arlington, a masseur, paid a penalty for practicing medicine without a license.

Salvador J. Abbatiello, an unlicensed chiropractor of South Amboy, paid the penalty for practicing medicine without a license.

Randal J. Brown, a registered pharmacist of Trenton, paid a penalty for practicing medicine without a license.

Howard Worne, a chemist of Newark, paid a penalty for practicing medicine without a license.

Ella Stevens, a "fortune teller" of Old Bridge, paid the penalty for practicing medicine without a license.

Charles Schaefer Jr., Oaklyn, for the fifth time paid the penalty for practicing medicine without a license.

NEW YORK

Society News.—Dr. Albert D. Kaiser, Rochester, addressed the quarterly meeting of the Ontario County Medical Society, Geneva, July 8, on "Rheumatic Disease in Childhood."——Dr. Karl M. Bowman, New York, addressed the Dutchess County Medical Society at the Harlem Valley State Hospital, New York, in June on "Military Psychiatry."——Dr. Henry C. Young, Hagaman, was recently elected an honorary member of the Montgomery County Medical Society after having been a member for fifty-three years.

New York City

Session on Pulmonary Diseases at Cornell.—A clinical session on pulmonary diseases will be held at Cornell University Medical College under the auspices of the Tuberculosis Sanatorium Conference of Metropolitan New York, October 8. The speakers will be Drs. Norman H. Plummer and Edgar Mayer on "Chemotherapy of Pulmonary and Pleural Infections" and "Management of the Early Infiltrative Tuberculous Lesion" respectively.

Internships at Hospital for Joint Diseases.—Six general two year rotating internships, three to begin July 1, 1942 and three to begin Jan. 1, 1943, are announced by the Hospital for Joint Diseases. An examination will be held at the hospital on October 23. Graduating students and graduates (unmarried men) of recognized medical schools are eligible. Applications should be addressed to the Director, Hospital for Joint Diseases, 1919 Madison Avenue.

Alumni Group Plans Program to Increase Life Expectancy.—Members of the class of 1900 of Columbia University College of Physicians and Surgeons have recently formed a committee on longevity to encourage and supervise medical examinations of the group in order to prolong the life expectancy and contribute to better health of each, it is reported. The committee prepared and distributed medical examination blanks and meets monthly to consider reports as they are returned and to recommend treatment if needed. The group believes that information gained from this program may be an important contribution to gerontology. Ninety-three members remain of a class of one hundred and seventy-five, it was said. The average age was reported to be 67. Facilities of the medical college at Columbia have been made available to the committee for examination of the members in the metropolitan area. Twenty per cent who live beyond commuting distance are examined by physicians in their own communities.

Emeritus Professors.—Dr. Eugene L. Opie, professor of pathology at Cornell University Medical College since 1931, has been made professor emeritus, according to *Science*. Before going to Cornell Dr. Opie was professor of pathology at Washington University School of Medicine, St. Louis, from 1910 to 1923 and professor and director of the department at the University of Pennsylvania School of Medicine, Philadelphia, from 1923 to 1931. At Pennsylvania he was also director of laboratories of the Henry Phipps Institute. John C. Torrey, Ph.D., professor of epidemiology, and Dr. Joshua E. Sweet, professor of experimental surgery, were also made professors emeritus. Dr. Torrey has been a member of the faculty for many years, serving as professor of hygiene, professor of public health and preventive medicine and since 1932 as professor of epidemiology. Dr. Sweet had held his professorship since 1926. Previously he had been on the faculty of the University of Pennsylvania School of Medicine (1906 to 1926).

NORTH DAKOTA

State Board Appointments. — Governor Moses recently appointed the following physicians to the North Dakota State Board of Medical Examiners: Drs. Cyril J. Glaspel, Grafton; William C. Fawcett, Starkweather, and Charles W. Schoregge, Bismarck.

First Evidence of Plague Infection in State.—Plague infection has been demonstrated in fleas collected, June 23, from ground squirrels shot in North Dakota, according to *Public Health Reports*. This is the first recorded evidence of plague infection in North Dakota, and the locality is believed to be the farthest east that so-called sylvatic plague (plague in wild rodents or their ectoparasites) has been recorded in the United States. In May 1939 plague infection was proved in tissue from a kangaroo rat trapped 10 miles west of Las Cruces, Dona Ana County, New Mexico, which was farther south and east than any other area in which plague in wild rodents had been demonstrated to exist in the United States prior to that date. This was also believed to be the first instance of the proof of plague infection among kangaroo rats in this country, *Public Health Reports* stated.

OHIO

District Meeting. — The annual meeting of the Eighth District of the Ohio State Medical Association was held at McConnellsville, June 19, with Drs. Claude S. Beck, Cleveland, and Leon Schiff, Cincinnati, as the speakers on "Heart Diseases Treated by Surgical Methods" and "Hematemesis and Melena—Newer Concepts" respectively.

Personal. — Dr. George W. Keil, formerly chief medical officer at the Ohio Penitentiary Hospital, Columbus, has been transferred to the Ohio Soldiers' and Sailors' Home near Sandusky as acting senior surgeon.——Ralph I. Dorfman, Ph.D., research assistant in physiologic chemistry at Yale University School of Medicine, New Haven, Conn., has been appointed assistant professor of biochemistry at Western Reserve University School of Medicine, Cleveland.—— Dr. Edward W. Laboe, Lima, has resigned as superintendent of the District Tuberculosis Hospital to become associate medical director of the Michigan State Sanatorium, Howell.

OKLAHOMA

Society News.—Drs. Ellis Moore and Joseph W. Kelso, Oklahoma City, addressed the Blaine County Medical Society in Watonga, June 20, on "A New Operation for Hemorrhoids" and "Vaginal Hysterectomy" respectively.—— Drs. Edward Halsell Fite and William Patton Fite, Muskogee, addressed the Pittsburg County Medical Society, McAlester, June 20, on "My Experiences in Transurethral Prostatic Resection" and "The Nailing of Intracapsular Fractures of the Neck of the Femur" respectively.——Dr. John M. Carson, Shawnee, addressed the Pottawatomie County Medical Society, Shawnee, August 16, on "Sulfanilamide and Its Derivatives with a Discussion of Sulfaguanidine."

OREGON

State Medical Meeting in Portland.—The sixty-seventh annual session and postgraduate assembly of the Oregon State Medical Society will be held in Portland, September 3-6, under the presidency of Dr. Karl H. Martzloff, Portland. Dr. Frank H. Lahey, Boston, President of the American Medical Association, will deliver an address on "Some of the Newer Developments in Medicine and Surgery," and three other guests will give three lectures each as follows:

Dr. George M. Curtis, Columbus, Ohio: Iodine and Calcium Metabolism in Thyroid Disease; Recent Advances in Thoracic Surgery; Recognition and Management of Acute Injury to the Chest.

Dr. Henry J. Tumen, Philadelphia: Diagnosis and Treatment of Jaundice; Management of Patient with Irritable Colon; Clinical and Gastroscopic Features of Chronic Gastritis.

Dr. Milton B. Cohen, Cleveland: Nature of Allergy, Its Pathology and Mechanisms of Its Production; Management of Patients with Asthma, Hay Fever and Other Allergic States; Growth Disturbances Produced by Allergy.

Panel discussions dealing with subjects in medicine, surgery, orthopedics, obstetrics and gynecology, dermatology and syphilology, allergy, psychiatry and radiology are also announced.

RHODE ISLAND

Personal.—Dr. William P. Shields, Providence, has been appointed epidemiologist in the state health department to succeed Dr. Harry B. Neagle, who resigned because of ill health. ——Dr. John E. Donley, Providence, has been named to an eleven member state council of defense by Governor McGrath. ——Dr. Henry A. Jones, Cranston, formerly superintendent of the State Infirmary, Howard, has been appointed assistant to the state director of social welfare.

SOUTH CAROLINA

Personal.—Dr. James C. Brabham, Walterboro, health officer of Colleton County, has been appointed health officer of Laurens and Union counties, succeeding Dr. Henry R. Perkins, Laurens. Dr. Lloyd W. Luttrell, Pickens, has been transferred from the health unit in Pickens County to succeed Dr. Brabham in Colleton County.

Society News.—Dr. James L. Hughes, Greer, among others, addressed the Greenville County Medical Society, Greenville, July 7, on "Borderline Deficiency Diseases."——Dr. William Halsey Barker, Baltimore, addressed the June meeting of the Florence County Medical Society, Florence, on "Uses and Abuses of the Sulfonamide Drugs." Dr. William R. Barron, Columbia, addressed the society, July 8, on "Prostatic Surgery."

VIRGINIA

Faculty Changes at University of Virginia.—Dr. Claude C. Coleman, clinical professor of neurological surgery at the University of Virginia Medical Department, Charlottesville, since 1937, has resigned. His successor will be Dr. William Gayle Crutchfield, Richmond, who has been associate clinical professor since 1937. Dr. John M. Meredith, assistant professor in the department, has also resigned and will now become associate professor of neurological surgery in the Medical College of Virginia, Richmond.

PUERTO RICO

Plan to Treat Rejected Selectees with Venereal Disease.—The director of the bureau of venereal diseases in the Puerto Rico Department of Health, Dr. Ernesto Quintero, San Juan, has recently given instructions to physicians in charge of the department's clinics for collaboration with selective service boards in bringing under treatment all men rejected by the boards because of venereal disease. The director recommends that a procedure be arranged by which health officials will be informed by the boards of all such cases. Treatment is to be offered free to the infected persons; their contacts are to be investigated and treatment also offered to any of those who are found to have venereal diseases. A follow-up system to keep patients under treatment was recommended, with a plan for reporting to the selective service boards any who stop treatment. Dr. Quintero recommended a similar program for workers in defense industries. Finally he urged an intensive educational program among selective service registrants, members of the armed forces and defense workers to keep them out of the hands of charlatans.

GENERAL

Changes in Status of Licensure.—The Board of Medical Examiners of Maryland recently reported the following action:

Dr. Henry L. Fahrney, Frederick, license restored February 11.

The Massachusetts Board of Registration in Medicine announces the following action:

Dr. Manford R. Spalding, Auburn, license suspended, July 11, for deceit in the writing of a narcotic prescription.

The Minnesota State Board of Medical Examiners, St. Paul, announces the following action:

Dr. Samuel R. Fraker, Minneapolis, license revoked, May 9, having pleaded guilty to a charge of performing an illegal operation.

Report on Encephalitis Outbreak.—Newspapers reported on August 13 that at least eighty-four deaths have been attributed to an outbreak of encephalitis in five midwestern states in the last two months. More than 800 persons were ill with the disease. Forty-six deaths and 400 cases were reported in North Dakota since the beginning of the outbreak; Minnesota, twenty-four deaths and 366 cases; South Dakota, ten deaths and 70 cases, and, since July 28, Nebraska, four deaths and Iowa, 10 cases. Four new cases were reported in Winnipeg, Canada, bringing the total of cases in Manitoba this year to 21, with three deaths.

Examinations in Obstetrics and Gynecology.—The American Board of Obstetrics and Gynecology announces that its next examination and review of case histories (part I) for group B candidates will be held in various cities of the United States and Canada on Jan. 3, 1942. Applications for admission to these examinations must be on file in the office of the secretary, Dr. Paul Titus, Pittsburgh, not later than October 1. The general oral and pathologic examinations (part II) for all candidates (groups A and B) will be conducted by the entire board in Atlantic City immediately prior to the 1942 meeting of the American Medical Association. The present fiscal year (1941-1942) marks the close of the two groups of classification of applicants for examination. Thereafter the board will have only one classification of candidates. Information and application blanks may be obtained from Dr. Titus, 1015 Highland Building, Pittsburgh.

Meeting of Railway Surgeons.—The fifty-second annual meeting of the American Association of Railway Surgeons will be held at the Palmer House, Chicago, September 8-10, under the presidency of Dr. Lucien Stark, Norfolk, Neb. The speakers will include:

Dr. Stanley J. Seeger, Milwaukee, Treatment of Burns.

Dr. M. Herbert Barker, Chicago, Chemotherapy—Sulfonamide Group.

Dr. Sumner L. S. Koch, Chicago, Tendon Suturing.

Drs. James E. M. Thomson and Charles F. Ferciot, Lincoln, Neb., Fractures of the Patella.

Dr. Spencer Wright, Salt Lake City, Newer Methods for the Repair of Inguinal Hernia.

Dr. Harold Feil, Cleveland, Cardiovascular Disabilities of Railway Employees—Problems of the Consultant: A Review of Eight Years' Experience.

Dr. Elisha S. Gurdjian, Detroit, Management of Traumatic Intracranial Hemorrhage.

Drs. Samuel J. Kopetzky and Ralph Almour, New York, Otoscopy in the Inflammations; A Clinic on Petrositis.

Bureau Plans Medical Aid to China.—The American Bureau for Medical Aid to China recently voted to spend $228,721 for immediate shipment of medical and other supplies to China. The fund was collected in part by the "Bowl of Rice" parties in California and also includes donations of $75,000 from the national committee of United China Relief and $45,000 from the China Emergency Relief Committee. Eight agencies carrying on relief work for China have recently combined with the joint title of United China Relief. Dr. Walter B. Cannon, Boston, is chairman and Donald D. Van Slyke, Ph.D., New York, is vice chairman of the medical division. The money will be used for support of hospitals for rehabilitation of bombed soldiers and civilians, for a first aid station for air raid victims in Chungking, for the emergency training schools for nurses and medical aides, for a medical library needed by the hospitals in their training work and for tools for transport repair shops for the Chinese Medical Relief Corps. Purchases will be made in consultation with the American Red Cross and the China Defense Supplies Commission recently established in Washington. The committee which will direct the expenditures consists of Drs. Frank Wang Co-Tui, chairman; Frank L. Meleney and Edward H. Hume, and Mr. Chih Meng. All are of New York.

Foreign Letters

PARIS

(From Our Regular Correspondent)

June 15, 1941.

Epidemic of Scabies

The incidence of scabies has tripled within the last few years. In 1938, 6,194 cases were observed in the Hôpital Saint Louis. This rose to 7,914 cases in 1939 and to 24,664 in 1940. There were three periods of exacerbation, the first among the mobilized, the second in the month of June at the time of massive evacuation of the populace and the third at the return of the evacuated in August.

In 1795, during the French Revolution, military centers of treatment for scabies were organized by decree. It was one of the problems of Napoleon to determine where to evacuate those affected with scabies. The present epidemic has permitted verification of the role which the germ carriers play in the dissemination of sarcoptes. Often a member of a family, to all appearance unaffected himself, by refusing to take precautionary measures spreads the contamination. Pignot pointed out before the Academy of Medicine the need of discovering these apparently innocuous carriers. The present scarcity of soap has had a direct influence on the epidemic. Various treatments have been employed at the Hôpital Saint Louis, such as Helmerich's ointment. However, fats have become so scarce in France that ointments will soon no longer be obtainable.

Wounds of the Head

Piquet and his associates reported recently to the Academy of Surgery their experiences with craniocerebral traumas in May 1940, at the time of the German invasion. Piquet was surgeon in chief of a center for cranial surgery situated on a bank of the LaManche River, a point distant from the combat zone. On May 18 this center found itself suddenly in the midst of a battle, and men with cranial wounds were rushed in. The hospital equipment was limited, and on the 19th electricity failed them. No longer could roentgenography, surgical diathermy or wound aspiration be done. Nor could foreign bodies be located in the wounds. Most of the wounded brought in for treatment had been injured ten days or two weeks previously and had been treated, more or less promptly, in another ambulance. Piquet's center was facing appalling conditions because of the scarcity of personnel and equipment and the pressure of time. The overworked surgeons were practically forced to adopt the surgical measures of the World War. Primary suture was done only on wounded men whose injuries did not date back beyond thirty-six hours. Fortunately, the sulfanilamide supplies were sufficient and massive doses were given. Failures were partly due to the inability to carry out the measures for the discovery of foreign bodies in the brain. Fatalities occurred in one third of the cases; only one third of these could be operated on in less than forty-eight hours after wounding. An additional factor was the need of moving the injured to make room for others. Piquet believes that foreign bodies in the brain should be removed as speedily as possible. This should be followed by prompt surgical intervention, done in one stage.

Technic for Determining Bactericidal Power of Blood

Bécard and Lepeut recently described before the Society of Medicine of Paris a simplified method for determining the bactericidal power of the blood. Blood specimens are obtained by digital puncture. No citrate is added. From a mother dilution representing a titer of 25,000,000 micro-organisms decimal dilutions in concentration ratios of 1, 10, 100 and 1,000 are prepared. These decimal dilutions are placed in four tubes and carefully mixed by shaking. By means of a graduated pipet a drop of the blood to be examined is deposited in each of the tubes and the latter incubated for thirty minutes at normal temperature (37 C.). Four different areas of the culture medium are inoculated with a drop of the dilution in a Petri dish containing peptonized agar-agar and incubated for twelve hours at normal temperature. The colonies of each area are then counted with a magnifying glass. The results are recorded in a diagram on which normal dilution figures (15, 150, 1,500, 15,000) are given on the abscissas and the bacterial count obtained from the colonies on the normal ordinates. The results are inscribed on the right or the left of the line representing the meeting place of abscissas and normal ordinates, the right indicating microbial decrease and hence a positive bactericidal power, the left indicating the opposite. The authors believe that by means of their diagram useful conclusions can be rapidly drawn regarding the surgical intervention proposed, the indications for immunotransfusion and in regard to the blood donors whose blood is highly bactericidal in view of the immunotransfusion.

Cold and Undernourishment

F. Bezançon discussed before the Academy of Medicine the dangers of undernourishment as it is affected by cold. The problem of heat regulation involves that of chemical thermoregulation and, in man, that of the peripheral circulation. Adaptation of the caliber of the blood vessels to the activity of their thermal functions varies in individuals. Urban dwellers who are not as extensively exposed to all the variations of outside temperatures lack good defense reflexes. Under the influence of cold, it is necessary for warm blooded animals to triple and quadruple the calory supply. The thermometric descent from 59 to 32 F. requires, for example, in the rat a tripling of the metabolism in relation to its basal metabolism. Aids in the process consist in shivering, in the chemical regulation of the body and in the support which the liver, the glands and the cells contribute. In human beings dwelling in our climate who do not modify a great deal the protective nature of their clothes, the thermal adjustment varies from 1,810 calories in summer to 3,000 calories with the arrival of cold.

Certain foods possess nutritional value against cold. Proteins, fats and carbohydrates may be substituted for one another to a certain extent; yet a vital minimum of each of these is indispensable. This involves the problem of equilibrium. Diets must contain protein, fat, mineral salts and amino acids. Individual physiologic differences as well as differences in the surrounding environment such as dryness, winds and sunshine are frequent. The frequent occurrence of chilblains during the recent severe cold demonstrated the role which food imbalance plays, for milk and butter are almost lacking at present in the French diet. Undernourishment, coupled with dietary imbalance, is particularly prejudicial to tuberculous persons in the developmental stage or with pneumothorax and to those affected with grave anemia. Physicians are now authorized to demand increased food allocations for persons with these disorders.

Psittacosis

Psittacosis has made its appearance in the Paris area. Fearing that the disease might spread, the public health department has made it notifiable. Psittacosis was first reported in Europe in 1930. The importation of parrots to France was prohibited at the time, and the bird shops were subjected to special inspections. In spite of these precautions, psittacosis did not altogether disappear. Isolated cases were encountered every year. Epidemiologic inquiries showed that these were due to the contamination of native breeding places. The source of these sporadic infections could not be traced, but it is now well

known that interhuman contamination is quite frequent. Diagnostic methods have been developed, but physicians in general often confuse the manifestations of psittacosis with those of influenza. Sacquépée, discussing this subject before the Academy of Medicine, believes that, if diagnosis was more searching, more cases of psittacosis would be found.

Congenital Dilatation of the Pulmonary Artery

Laubry and Routier recently reported to the Academy of Medicine their findings in 39 cases of a condition which they regard as congenital dilatation of the pulmonary artery but which Cossio of Buenos Aires had described clinically and roentgenologically as interauricular communication. Eight of their cases came to necropsy. The symptomatology is diverse, yet the roentgenologic signs are constant enough and similar to those disclosed in the roentgenogram to permit grouping them together. The description of the roentgenologic silhouette shows a significant right border, an arc of average projection, strongly expansive pulmonary hilus shadows and a smaller invisible aortal semicircle. Clinically, diastolic and systolic murmurs were noted. Functional signs, especially cyanosis, were delayed. The evolutionary trend was generally toward bronchial dilatation, to chronic emphysema with thoracic blockage or toward pulmonary tuberculosis.

RIO DE JANEIRO

(From Our Regular Correspondent)

June 15, 1941.

Cardiovascular Diseases in Rio de Janeiro

The cardiovascular diseases offer considerable difficulty in an appraisal of their importance, because many of the factors involved are ignored. In Rio de Janeiro exact studies on the incidence of these diseases have been lacking, though mortality statistics have been kept since 1903, which year marked the beginning of the modern era of public health in Brazil. Publication of the mortality data for the last fifteen years has shown that deaths from cardiovascular diseases increased from 9.41 per cent of the deaths from all causes in the period 1926-1930 to 11.37 per cent in the period 1936-1940, and the crude specific death rate similarly increased from 165 to 189 per hundred thousand of population, an increase of 14.54 per cent.

More interesting is the study of the morbidity by Prof. Pedro Da Cunha of the Fluminense Medical School and the Gaffrée-Guinle Hospital, relating to 40,186 people attending the outpatient clinic of that hospital from 1926 to 1939. Of this total, 32,830 patients, or 81.70 per cent, were classified as afflicted by diseases of the cardiovascular system. The patients were 37.74 per cent male and 62.26 per cent female, 80.17 per cent of Brazilian nationality and 19.83 per cent foreign, 64.16 per cent white and 35.89 per cent Negro, 31.26 per cent single, 54.74 per cent married and 14.00 per cent widowed and divorced, 7.68 per cent under 20 years of age, 76.99 per cent between 20 and 49 and 16.43 per cent 50 years and over. The aneurysms are only 0.40 per cent of the grand total. Some features of the study need emphasis. Essential hypertension has been found in only 0.29 per cent of the cases and hypotension in 0.45 per cent. Syphilis was the cause of cardiovascular disease in 24 per cent of the patients, and in about two thirds the specific lesion was in the aorta. Syphilis was much more frequent as a cause of valvular diseases than rheumatic conditions. The ratio between syphilis and rheumatism is about 2:1 for the aortic lesions and about 1:1 for the mitral lesions. The Wassermann reaction was positive in 24.95 per cent of the cases of aortic lesions and in 22.75 per cent of the mitral lesions. Rheumatic conditions alone were found in 10.80 per cent of the cases, and in 2.20 per cent associated with syphilis. As a probable explanation, Rio de Janeiro has a tropical climate, where rheumatic diseases are rather rare and syphilis is very prevalent.

It is interesting to note at the same time the principal features of a report by Dr. Amadeu Fialho, pathologist of the public health laboratory of the city, on the results of 3,474 necropsies in which 890 cases of cardiovascular diseases were found. Of the 890 deaths attributed to cardiovascular diseases, atherosclerosis accounted for 322 cases, cardiac hypertrophy for 168, diseases of the pericardium for 81, syphilitic aortitis for 70, valvular diseases for 69, endocarditis for 63, aneurysm of the thoracic aorta for 40 and sclerosis of the myocardium for 10.

Still another contribution on the subject is that of Drs. Aloysio De Paula and Francisco Benedetti, who examined, in the Health Centers of Rio de Janeiro, 28,293 office and shop employees with the use of the miniature roentgenogram and found unknown cases of heart disease in 0.8 per cent, and unknown aortic disease in 3.9 per cent.

Marriages

CHARLES WHITE MILLENDER, Asheville, N. C., to Miss Dorothy Thompson Aiken of Columbia, Tenn., recently.

WILLIAM CHESTER, Mamaroneck, N. Y., to Miss Anne Mitsak of Bridgeport, Conn., in New York, May 24.

JOHN MILTON STRAIT JR., Columbus, Ohio, to Miss Anne Louise Ferguson of Mount Vernon, June 19.

ROBERT MCCLELLAN JAMES, Louisville, Ky., to Miss Lois Livingston of Hazard in Covington, June 14.

ALVA DUCKETT DAUGHTON, East Falls Church, Va., to Miss Vera Alice Hanson of Richmond, July 18.

HAROLD RAWLING PRATT-THOMAS to Miss Mary Porcher Douglas, both of Charleston, S. C., July 2.

GEORGE ASHBY WINSTEAD to Miss Jacqueline Gainer Denson, both of Rocky Mount, N. C., June 17.

FRANCIS PATRICK O'LINN, Youngstown, Ohio, to Miss Margaret Ellen Rataiczak of Troy, June 28.

JOHN WASHINGTON CLARK, Front Royal, Va., to Miss Sallie McArthur Mason of Ridgeway, June 24.

MAURICE J. SMALL, Parsons, W. Va., to Miss Sylvia Cantor of New Rochelle, N. Y., March 25.

WILLIAM CARLETON SMITH, Lockhart, Texas, to Miss Maybell Hardie of Fort Worth recently.

WALDEMAR RICHARD AGRICOLA to Miss Virginia Berry, both of Newcomerstown, Ohio, in July.

NORMAN DOUGLAS ELLIS JR., Martin, S. C., to Miss Martha Alice Bennett of Dillon, June 28.

BENJAMIN FRANKLIN HOOPES, Bloomington, Ill., to Miss Frances Kelly of Chicago recently.

SAMUEL JOSEPH CAMPBELL, Bucyrus, Ohio, to Miss Dorothy Isabel Cole in Fremont, June 21.

WILLIAM ST. JULIEN JERVEY to Miss Susan Amelia Sprague, both of Tryon, N. C., June 30.

WILLIAM HENRY BANDY, Lincolnton, N. C., to Miss Pauline Pope of Linwood, June 21.

HUGH I. CONN, Newman, Ill., to Miss Virginia Thompson at Danville, Ind., June 12.

RUSSELL C. LONG, Zanesville, Ohio, to Miss Isabel Hepler of Mount Vernon in June.

GILBERT THOMAS RANSOM to Mrs. Robley Wilson, both of Fairfield, Ill., in June.

HARLIN G. KNIERIM, Detroit, to Miss Florence Stevens of Galion, Ohio, recently.

ABRAHAM W. FELDMAN to Miss Minerva Shapiro, both of Chicago, August 10.

SOL L. LOWENSTEIN to Miss Corinne Cohn, both of Nashville, Tenn., July 2.

STANLEY H. MACHT, Crewe, Va., to Miss Naomi Newman of Danville, July 1.

PAUL AXTELL BUNN, Cleveland, to Miss Elizabeth Maxwell of Akron, June 14.

Deaths

John Price Crozer Griffith ✠ Philadelphia; University of Pennsylvinia Department of Medicine, Philadelphia, 1881; emeritus professor of pediatrics at his alma mater and the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania; member of the American Pediatric Society; for many years treasurer of the Association of American Physicans; past president of the Philadelphia Pediatric Society; corresponding member of the Société de pédiatrie de Paris; served at various times and in various capacities on the staffs of St. Christopher's Hospital for Children, Children's Hospital, Women's Hospital, Jewish Hospital, Abington (Pa.) Memorial Hospital, Misericordia Hospital and the Babies Seashore Hospital; author of several volumes on children's diseases; aged 85; died, July 28, at his summer home in Devon.

Edward Frankel Jr. ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1905; instructor in otolaryngology at his alma mater from July 1, 1930 to June 30, 1932; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; past president of the American Stomatological Association; veteran of the Spanish-American and World wars; on the staffs of the Broad Street Hospital and the Presbyterian Hospital; associate editor of the *Journal of Dental Research* from 1932 to 1937; aged 60; died, July 3, of embolism following an appendectomy.

Frederick Eugene Hopkins ✠ Springfield, Mass.; University of the City of New York Medical Department, 1884; member of the American Laryngological Association and the American Laryngological, Rhinological and Otological Society; past president of the New England Otological and Laryngological Society; fellow of the American College of Surgeons; for many years member of the school committee; at various times on the staff of the Springfield Hospital, Noble Hospital, Westfield and the Memorial Hospital, Brattleboro, Vt.; aged 83; died, July 1, of cerebral embolism and hypertrophy of the prostate.

Edmund Sheppard Ferguson ✠ Oklahoma City; Detroit College of Medicine, 1895; emeritus professor of ophthalmology at the University of Oklahoma School of Medicine; one of the founders and past president of the Oklahoma City Academy of Medicine; past president of the Oklahoma State Medical Association; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; on the staffs of St. Anthony's, Wesley and Oklahoma City General hospitals; aged 70; died, June 28, of coronary occlusion.

Frank Everett Kittredge ✠ Nashua, N. H.; University of Pennsylvania Department of Medicine, Philadelphia, 1885; member of the American Academy of Ophthalmology and Otolaryngology and American Laryngological, Rhinological and Otological Society; past president of the New England Otological and Laryngological Society; fellow of the American College of Surgeons; on the staffs of St. Joseph's and Nashua hospitals; aged 79; died, July 8, of heart disease in Newfoundland while on a fishing trip.

Caspar W. Sharples ✠ Seattle; University of Pennsylvania Department of Medicine, Philadelphia, 1888; member of the Pacific Coast Surgical Association and past president of the North Pacific Surgical Association; fellow of the American College of Surgeons; past president of the city school board; past president of the Washington State Medical Association; on the staff of the Children's Orthopedic Hospital; aged 75; medical superintendent of the Seattle General Hospital, where he died, July 15.

William Hurley Strietmann ✠ Oakland, Calif.; Medical College of Ohio, Cincinnati, 1905; at one time instructor in obstetrics and demonstrator of physiology at his alma mater; fellow of the American College of Physicians; past president of the Alameda County Medical Society; member of the Alameda County Institutions Commission; chairman of the medical department of the Alameda County Hospital; on the staff of the Peralta Hospital; aged 60; died, July 14, of coronary disease.

George Kingsley Olmsted ✠ Denver; Denver and Gross College of Medicine, 1903; past president of the state board of health; fellow of the American College of Physicians; on the staffs of the Denver General and St. Luke's hospitals; lieutenant colonel, medical reserve corps, United States Army, retired; aged 69; died, June 25, in St. Luke's Hospital of coronary thrombosis and diabetes mellitus.

Willard Clifton Hearin, Greenville, S. C.; Medical Department of Tulane University of Louisiana, New Orleans, 1910; member of the South Carolina Medical Association and the South Atlantic Association of Obstetricians and Gynecologists; past president of the Greenville County Medical Society; served during the World War; aged 54; died, July 9, in St. Francis Hospital of angina pectoris.

John Bell, New Glasgow, N. S., Canada; McGill University Faculty of Medicine, Montreal, Que., 1898; for many years secretary of the Pictou County Medical Association; for many years a member of the legislative council of Nova Scotia; on the staff of the Aberdeen Hospital; aged 65; died, May 27, in the Victoria General Hospital, Halifax.

John Purney, New Britain, Conn.; Baltimore Medical College, 1906; member of the Connecticut State Medical Society; served with the Canadian Army during the World War; on the staff of the New Britain Hospital; aged 62; died, July 18, of coronary thrombosis while on his vacation in Shelburne, Nova Scotia, Canada.

Rollin M. Pelton, Richford, Vt.; University of Vermont College of Medicine, Burlington, 1888; member of the Vermont State Medical Society; for many years member of the school board and health officer; formerly member of the state legislature; aged 75; died, June 4, in the Mary Fletcher Hospital, Burlington, of arteriosclerosis.

Aaron A. McKelvey, Van Buren, Ark.; Arkansas Industrial University Medical Department, Little Rock, 1894; member of the Arkansas Medical Society; formerly a member of the Veterans Administration; city and county health officer; aged 74; died, May 21, in a hospital at Fort Smith of heart disease.

Bernard Rubenstein ✠ Dallas, Texas; Baylor University College of Medicine, Dallas, 1922; assistant professor of clinical gynecology at his alma mater; fellow of the American College of Surgeons; on the staffs of the Parkland and Baylor hospitals; aged 51; died, June 12, of coronary occlusion.

John Glasscock Tye, Barbourville, Ky.; University of Louisville Medical Department, 1909; member of the Kentucky State Medical Association; member of the board of health; aged 60; died, June 21, in the Kentucky Baptist Hospital, Louisville, of carcinomatosis.

John Edward Lawrence Walsh, Evanston, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1886; Rush Medical College, Chicago, 1887; aged 79; died, July 1, in St. Luke's Hospital, Chicago, of coronary thrombosis and carcinoma of the stomach.

Cleal Giles Hissong, Hamler, Ohio; Eclectic Medical College, Cincinnati, 1915; member of the Ohio State Medical Association; mayor; served during the World War; member of the board of education; aged 50; died, June 29, of coronary thrombosis.

Chauncey Goodrich Wright, St. Louis; Washington University School of Medicine, St. Louis, 1905; member of the Missouri State Medical Association; served during the World War; aged 67; died, June 10, in the Missouri Baptist Hospital.

Thomas Gibson, Kingston, Ont., Canada; University of Edinburgh Faculty of Medicine, Scotland, 1894; professor of the history of medicine, Queen's University Faculty of Medicine; aged 75; died, July 2, in the Kingston General Hospital.

Bertha Wagner Stark, Los Angeles; Hahnemann Medical College of the Pacific, San Francisco, 1895; College of Physicians and Surgeons of San Francisco, 1901; aged 76; died, June 28, in San Bernardino of acute dysentery.

Jacob Moon Anderson, Sardis, Miss.; Memphis (Tenn.) Hospital Medical College, 1898; member of the Mississippi State Medical Association; town health officer; past president of the school board; aged 71; died, July 8.

Joseph Fulgence Archambault, West Warwick, R. I.; College of Physicians and Surgeons, Baltimore, 1905; member of the Rhode Island Medical Society; aged 60; died, June 26, in Bridgton, Maine, of coronary thrombosis.

John Lewis Bishop, Niagara Falls, N. Y.; University of Buffalo School of Medicine, 1903; served during the World War; formerly city health officer; aged 64; died, June 10, in the Memorial Hospital of coronary sclerosis.

Josie C. Kennedy Diederich, Rochelle, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; member of the Illinois State Medical Society; aged 68; died, June 7.

Clifford Sater, Cincinnati; Miami Medical College, Cincinnati, 1901; served during the World War; aged 70; died,

June 28, in San Diego, Calif., of hypostatic pneumonia, diabetes mellitus and fracture of the femur.

Frank William Knittel ✠ Brunswick, Ohio; St. Louis University School of Medicine, 1928; on the staff of the Community Hospital, Berea; aged 40; died, June 26, of injuries received in an automobile accident.

John Whitworth Harrison, Kansas City, Mo.; Medical Department of Tulane University of Louisiana, New Orleans, 1899; veteran of the Spanish-American War; aged 64; died, June 10, of chronic myocarditis.

William Henry Haines, Audubon, N. J.; Jefferson Medical College of Philadelphia, 1912; served during the World War; for many years member of the city board of health; aged 55; died, July 5, of heart disease.

Hjalmar V. Barclay, Corona, N. Y.; University of the City of New York Medical Department, 1893; aged 81; died, June 23, in the Roosevelt Hospital, New York, of arteriosclerosis and heart disease.

Joseph Alan Corson, Wilkes-Barre, Pa.; Jefferson Medical College of Philadelphia, 1921; member of the Medical Society of the State of Pennsylvania; aged 46; died, May 25, of cerebral hemorrhage.

James Clair Ash, Lake Andes, S. D.; Barnes Medical College, St. Louis, 1899; member of the South Dakota State Medical Association; formerly member of the state legislature; aged 70; died in July.

Albert C. McClanahan ✠ Los Angeles; Rush Medical College, Chicago, 1889; member of the Colorado State Medical Society; aged 76; died, June 15, at Santa Barbara, Calif., of coronary thrombosis.

U. S. Grant Sparks, Pitman, N. J.; Medico-Chirurgical College of Philadelphia, 1895; aged 68; died, May 26, in the New Jersey State Hospital, Trenton, of coronary occlusion and arteriosclerosis.

Constantine A. Carusos, New York; National University of Athens School of Medicine, Greece, 1902; aged 58; died, June 8, in Tarpon Springs, Fla., of cerebral hemorrhage and heart disease.

Fred Hugh Van Tassell, Oakland, Calif.; University of California Medical Department, San Francisco, 1904; aged 62; died, June 29, in the Berkeley (Calif.) Hospital, of cerebral hemorrhage.

Fred Clark Taylor ✠ Peru, Ill.; Medical College of Indiana, Indianapolis, 1894; aged 68; on the staff of the People's Hospital, where he died, June 29, of peritonitis following an operation.

Dallas Curtice Johnson, San Antonio, Texas; University of Texas School of Medicine, Galveston, 1926; served during the World War; aged 43; died, June 24, of pulmonary tuberculosis.

George Byron Walrath, Los Angeles; University of Southern California College of Medicine, Los Angeles, 1895; aged 75; died, June 20, of carcinoma of the pyloric end of the stomach.

Thomas Ives Byrne, Yarmouth, N. S., Canada; Bellevue Hospital Medical College, New York, 1894; for many years deputy minister of health of Nova Scotia; aged 67; died, May 29.

George Augustus Porter Boulden, Staten Island, N. Y.; Long Island College Hospital, Brooklyn, 1897; aged 78; died, May 12, in Montgomery township, N. J., of chronic myocarditis.

Ernest Franz, Berne, Ind.; Hahnemann Medical College and Hospital, Chicago, 1893; member of the Indiana State Medical Association; aged 76; died, June 27, of cerebral hemorrhage.

Felton D. Watts, Portland, Ore.; Detroit College of Medicine, 1904; member of the Oregon State Medical Society; aged 75; died, June 17, of coronary occlusion and hypertension.

Charles Anthon Walters, Santa Fe, Tenn.; University of Tennessee Medical Department, Nashville, 1896; served during the World War; aged 70; died, June 10, of myocarditis.

Thomas James Gallagher, Paterson, N. J.; Temple University School of Medicine, Philadelphia, 1923; aged 47; died, June 30, in St. Joseph's Hospital of coronary occlusion.

Abel W. Truesdell, Lake Orion, Mich.; Saginaw (Mich.) Valley Medical College, 1902; for many years health officer; aged 83; died, June 28, of carbolic acid taken accidentally.

Edward Lipman Efroymson, Bell, Calif.; Indiana University School of Medicine, Indianapolis, 1935; aged 30; died, June 12, of an overdose of a sedative, self administered.

George L. Brooks ✠ Chicago; Chicago Homeopathic Medical College, 1901; on the staff of the Chicago Memorial Hospital; aged 62; died, July 2, of coronary occlusion.

Raymond James Stoup ✠ Syracuse, N. Y.; Syracuse University College of Medicine, 1900; aged 63; died, June 11, in the University Hospital of myelogenous leukemia.

John Wesley Newlove, Los Angeles; Detroit College of Medicine, 1902; served during the World War; aged 61; died, June 29, of cirrhosis of the liver and edema.

William Rice Silverstein, Bradley Beach, N. J.; Baltimore Medical College, 1903; aged 58; died, June 21, in the Beth Israel Hospital, Newark, of cholelithiasis.

Bertha Olive Anderson ✠ Pittsfield, Mass.; University of Kansas School of Medicine, Kansas City, Kan., 1911; aged 58; died, June 25, of coronary thrombosis.

Gustav Baar, Portland, Ore.; Medizinische Fakultät der Universität Wien, Austria, 1897; aged 68; died, July 6, of hypertensive cardiovascular disease.

John Henry Weckel, Syracuse, N. Y.; University of the City of New York Medical Department, 1879; aged 83; died, June 30, of cerebral hemorrhage.

John J. Johnson, Harrison, Ark.; Marion-Sims College of Medicine, St. Louis, 1896; member of the Arkansas Medical Society; aged 80; died in June.

Calbert H. Beach, Glencoe, Okla.; Missouri Medical College, St. Louis, 1889; Barnes Medical College, St. Louis, 1898; aged 79; died, May 15.

Ella Pearson Sumner, Hastings, Neb.; Omaha Medical College, 1895; member of the Nebraska State Medical Association; aged 94; died, June 10.

James M. Tyson, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1892; aged 79; died, June 13, of cerebral thrombosis.

Michael Joseph Donovan, Perry, Iowa; John A. Creighton Medical College, Omaha, 1907; aged 68; died, June 12, of coronary thrombosis.

Harvey James Clements ✠ Salem, Ore.; New Orleans University Medical College, 1892; aged 72; died, June 25, of coronary occlusion.

Thomas P. Mitchell, Lincolnton, Ga.; University of Georgia Medical Department, Augusta, 1887; aged 88; died, April 9, of mitral insufficiency.

William Wallace Aldrich, Wevertown, N. Y.; Dartmouth Medical School, Hanover, N. H., 1878; aged 87; died, June 24, of arteriosclerosis.

Hubert Adolphus Thomas, Princeton, Ky.; Meharry Medical College, Nashville, Tenn., 1930; aged 41; died, June 17, of acute endocarditis.

Ralph Milburn Burton ✠ Toledo, Ohio; University of Louisville (Ky.) School of Medicine, 1925; aged 41; died, June 23, of carcinoma.

William H. Buchan, Gilmer, Texas; Memphis (Tenn.) Hospital Medical College, 1902; aged 63; died, June 2, of chronic nephritis.

Laurance Victor Croft, London, Ont., Canada; McGill University Faculty of Medicine, Montreal, Que., 1903; aged 64; died, May 19.

John Donald Stewart, Calgary, Alta., Canada; McGill University Faculty of Medicine, Montreal, Que., 1911; aged 56; died, May 23.

Ernest Sullivan, Oklahoma City; Barnes Medical College, St. Louis, 1907; aged 59; was found dead in bed, June 1, of heart disease.

Mark Hilton Moore, Athens, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1903; aged 68; died, May 26.

Frederick E. Dillenbeck, El Dorado, Kan.; University Medical College of Kansas City, Mo., 1896; aged 74; died, June 5.

Douglas Hart, Montgomery, Ind.; Louisville (Ky.) Medical College, 1891; aged 80; died, July 1, of carcinoma of the face.

Squire H. Redmon, Tipton, Mo.; St. Louis Medical College, 1880; aged 87; died, May 7, of chronic interstitial nephritis.

Albert David Faust, Bala-Cynwyd, Pa.; Jefferson Medical College of Philadelphia, 1894; aged 69; died, June 9.

Linton S. Archer, Atlanta, Ga.; Maryland Medical College, Baltimore, 1908; aged 57; died, July 4.

Bureau of Investigation

THE MACHINE AGE MOVES IN ON SEX

Contraption Promoted as Sexual Cure-All Declared Fraudulent

For many years mechanical devices and nostrums have been the subjects of United States Post Office fraud orders. During recent years this department of THE JOURNAL has given little space to what, for want of a better term, are called "sex frauds"—that is, those devices and "cures" promoted solely for the treatment of imaginary or real sexual deficiencies.

Now the Post Office Department has issued a fraud order against a concern which promoted a mechanical device like something out of Dr. Seuss or Rube Goldberg. Under the names Grindley and Company and Matrimonial Body Support Company, Missoula, Mont., one Thomas C. Grindley advertised and sold through the mails a booklet entitled "A Positive Solution to Many of the Problems of Coitus in Married Life." The memorandum of charges served by the Post Office Department on Mr. Grindley alleged that the following pretenses, representations and promises were false and fraudulent: That the booklet correctly advises how to restore "strength, pep, vitality and endurance" to sexually weak men, regardless of age or physical condition; that it advises how effectively to correct "premature ejaculation"; that it correctly advises purchasers how to continue the sexual act with perfect satisfaction for an hour or more and maintain an erection of the male sexual organ during that time; that the booklet correctly advises purchasers how to retard the climax of the sexual act as long as desired "without fatigue," and how to perform the sexual act "as often as desired" and leave the user "fresh as a daisy afterward"; further, that it advises how to prevent "frigidity" in women and furnishes effective information on "birth control."

Examination of the text of the booklet shows that the results mentioned were to be obtained by the construction of a device designed to support the weight of the male during the act of coitus. This extraordinary construction was to be made by the purchasers of the booklet according to the specifications set forth in the last four pages. According to the fraud order, "it consists of two metal braces, to be placed approximately two feet apart, connected by a metal rod, suspended from which is a heavy canvas or linen upon which the body of the male is to be placed during the act of sexual intercourse. For those who do not wish to make their own support as described in the booklet, the promoter offers to make one and furnish the same for prices ranging from $3.50 to $4.00."

Also included in the booklet are the following directions:

HOW TO USE

Be sure that the cross or tie bar marked "O" clears the body of the woman by at least one inch (below the breasts) when the entire weight of the man is upon the support.

Next get into position and adjust the edge of the fabric support so that it is just above the woman's pelvis, and supports the entire abdomen of the man.

Then tilt the fabric support so that the man's weight is barely raised off the woman's abdomen. One adjustment is generally final.

Do not cut down the strength of the materials suggested. The support has to be strongly made. Use 10 ounce canvas or very strong linen, re-enforced to make fabric support.

The picture of the human animal endeavoring to propagate the species while at the same time manipulating this combination hoist and viaduct is something that startles the imagination. Expert testimony of government witnesses was nevertheless apparently necessary to show the wide variety of etiologic factors of the various disorders which this device was claimed to correct. It was so obviously a scheme for obtaining money through the mails by means of false and fraudulent pretenses, representations and promises that the Solicitor recommended that a fraud order be issued. The Acting Postmaster-General on April 30, 1941 issued Order No. 15486 against Grindley and Company, the Matrimonial Body Support Company and their officers and agents as such.

Correspondence

HEMOGLOBIN-RED BLOOD CELL RATIO

To the Editor:—In an article entitled "A Simple Hemoglobin-Red Blood Cell Ratio to Replace the Color Index" (THE JOURNAL, May 17, p. 2258) Isaacs criticizes the value of the color index figure of the blood. He states: "However, the lack of single 'normal' figures for the percentage of hemoglobin and red blood cell counts, as well as the differences in males and females, has always made the number somewhat arbitrary. With the advent of hemoglobinometers in which 100 per cent corresponds to 13.5, 14, 15.6 or 17 Gm., the problem is further complicated by the difference in readings of the percentages."

These statements indicate that Isaacs' method of determining the color index does not conform to that commonly employed, and because it may lead to further confusion the statements should be corrected. The color index is determined by dividing the percentage of the normal hemoglobin value calculated from the hemoglobin reading obtained by the percentage of the normal erythrocyte level calculated from the erythrocyte count obtained. Consequently it makes no difference whether the patient is male or female or what number of grams of hemoglobin corresponds to 100 per cent on the hemoglobinometer reading.

It is true that there is some slight divergence of opinion in regard to what the normal hemoglobin and erythrocyte levels are for male and female patients and at various ages, but these differences will affect the final calculation little. If one assumes that the average normal hemoglobin and erythrocyte levels are 15.5 Gm. and 5,200,000 for males and 14.5 and 4,800,000 for females, one may readily see that the normal color index in each case is 1; that is, 100 per cent/100 per cent = 1. In each case, each figure represents 100 per cent of normal irrespective of the sex or, in the case of the hemoglobin figures, what amount of hemoglobin corresponds to 100 per cent on the scale used.

To illustrate, using Isaacs' figures: 9.3 Gm. of hemoglobin is 60 per cent of the normal male ($9.3/15.5 \times 100 = 60$ per cent) and 64.2 per cent of the normal female ($9.3/14.5 \times 100 = 64.2$ per cent) hemoglobin; 2,800,000 erythrocytes per cubic millimeter is 53.8 per cent of the normal male ($2{,}800{,}000/5{,}200{,}000 \times 100 = 53.8$) and 58.4 per cent of the normal female ($2{,}800{,}000/4{,}800{,}000 \times 100 = 58.4$) erythrocyte level. Therefore, $60/53.8 = 1.11$ color index for the male and $64.2/58.4 = 1.10$ color index for the female. To carry the calculations further, Isaacs uses the same erythrocyte level with 7 Gm. of hemoglobin. Calculations made in the same manner show color index values for the male $45.2/53.8 = 0.84$ and for the female $48.2/58.2 = 0.83$. It is obvious from these figures, readily computed on the slide rule, that in the first example the color index is approximately 1, whereas in the second example it is below normal, indicating an iron deficiency whether or not the patient is male or female and without reference to the percentage reading obtained from the hemoglobinometer used. This is an excellent example of the desirability of reporting hemoglobin values in grams rather than in percentage unless the number of grams represented by 100 per cent is stated. When this is done, there should be no confusion in regard to the hemoglobin content or the color index figure in any specimen of blood. Present day means available for determining the hemoglobin and erythrocyte levels are far superior to those in use a few years ago, so that greater accuracy is possible, thus making the color index figure a much more reliable and valuable one than it was a few years ago.

WILLIAM P. MURPHY, M.D., Boston.

[NOTE.—The preceding letter was referred to Dr. Isaacs, who replies:]

To the Editor:—Dr. Murphy assumes that the average "normal" hemoglobin and erythrocyte levels are 15.5 Gm. and 5,200,000 for males and 14.5 Gm. and 4,800,000 for females. This illustrates my point exactly and demonstrates just what I wished to avoid. These standards of normal (1) are purely arbitrary and (2) differ with different workers and authors and in different parts of the country. I certainly agree with Dr. Murphy that the reporting of hemoglobin in grams is more desirable than in percentage, and my formula was merely a way by which a physician without a slide rule could get a mental image of whether the number of grams was high, low or comparable to the changes in the individual patient's red blood cell count. It is easy to multiply the number of grams of hemoglobin by 3 and see whether this number is higher than, equal to or lower than the first two figures of the red blood cell count.

RAPHAEL ISAACS, M.D., Chicago.

PRESCRIPTION OF SULFONAMIDES

To the Editor:—Do you not think a warning on the unjustifiable, promiscuous and indiscriminate prescribing of the sulfonamides in an effort to curb such unwarranted practice might be timely and perhaps serve a good purpose?

A few years ago at a general medical meeting I was the only otolaryngologist of three present who spoke against such practice. The other two and many general practitioners said that they prescribed sulfonamide derivatives as a routine in the home in every case of acute suppurative otitis media. I decried it then, and all the more do I do so now after two years have passed and I have seen the results.

Only yesterday I had a typical example of their misuse—and this is not an isolated case: A woman aged 20 had acute suppurative otitis media with a spontaneous perforation on June 15, 1941. The next day her otologist placed her on sulfanilamide 2 tablets every four hours for twenty-five doses. The ear discharged freely for about two weeks and then stopped, with return of the otalgia. Her otologist performed a myringotomy, following which the ear again discharged freely until July 13, when it stopped with return of pain, and when I saw her for the first time on the evening of July 15 she had advanced acute mastoiditis. I did a mastoidectomy on her the next day. The whole mastoid was filled with pus and granulations, and there was a small fistula through the outer table. Necrosis of the bone was far advanced and the dura was exposed and bathed in pus. It was evident that mastoiditis had existed for some time, the symptoms masked by sulfanilamide, and if it had not perforated through the outer mastoid wall meningitis, an extradural abscess or a septic sinus thrombosis would have developed all unsuspected.

For the more than thirty years during which I have practiced otology before the advent of the sulfonamides I have seen 80 per cent of patients with acute suppurative otitis media get well without chemotherapy. If sulfanilamide is used, it should be saved for those patients who show after perhaps a week following the opening of the tympanum that they are not doing well. Then it should be given to the proper blood concentration and under such supervision that daily examinations of the blood can be made and should be continued in modified dosage for one week after all symptoms have subsided.

Why subject this 80 per cent needlessly to a toxic drug with its attendant dangers, often given in inadequate doses without proper supervision and stopped all too soon? More often than not, it does more harm than good. It would seem that the time has come when the indiscriminate, unwarranted and pernicious use of this drug should be stopped.

GEORGE W. STIMSON, M.D., Warren, Ohio.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

CHICAGO, Feb. 16-17, 1942. Council on Medical Education and Hospitals, Sec., Dr. William D. Cutter, 535 North Dearborn Street, Chicago.

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, August 16, page 554.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Sept. 15-17. Part III. Baltimore and New York City, October; Boston, November. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written.* Nov. 3. Final date for filing application is Sept. 23. *Oral.* Dec. 12-13. Final date for filing application is Nov. 8. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 20. Final date for filing application is Sept. 1. *Oral.* April, in advance of the meeting of the American College of Physicians and June, in advance of the meeting of the American Medical Association. Final date for filing application is Oct. 20. Sec., Dr. William S. Middleton, 1301 University Ave,, Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I. Group B.* Various centers, Jan. 3. Final date for filing application is Oct. 6. *Oral. Part II. Groups A and B.* Atlantic City, May or June. Final date for filing application is March 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Chicago, Oct. 18. *Written.* March 7. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Washington, January. Final date for filing application is Nov. 1. Sec., Dr. Guy A. Caldwell, 3503 Prytania St., New Orleans, La.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Philadelphia, March or April, at the time of the Region I meeting of the American Academy of Pediatrics. Cleveland, May, at the time of the Region III meeting of the American Academy of Pediatrics. Los Angeles, May, at the time of the Region IV meeting of the American Academy of Pediatrics. *Written.* Locally, approximately 6 weeks in advance of the date of oral examination. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, Dec. 19-20. Final date for filing application is Oct. 5. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF SURGERY: *Written. Part I.* Various centers, Oct. 6. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* Various centers, December. *Oral.* Chicago, February. Final date for filing application is Nov. 1. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Maine March Report

The State of Maine Board of Registration of Medicine reports the written examination for medical licensure held at Portland, March 11-12, 1941. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Twenty candidates were examined, 13 of whom passed and 7 failed. Two physicians were licensed to practice medicine by reciprocity and 4 physicians so licensed on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Rush Medical College		(1940)	83
Boston University School of Medicine		(1940)	80
Harvard Medical School		(1940)	80, 81
Tufts College Medical School		(1933) 75.6, (1940)	78
University of Pennsylvania School of Medicine		(1939)	82
Laval University Medical Faculty, Montreal		(1909)	75.4
McGill University Faculty of Medicine		(1940)	78
Medizinische Fakultät der Universität Wien		(1929) 76, (1938)	75.3
Faculté Francaise de Médecine de l'Université de St. Joseph, Beyrouth		(1936)	83
Universität Bern Medizinische Fakultät		(1936)	76

School	FAILED	Year Grad.
Boston University School of Medicine		(1936)
Tufts College Medical School		(1935)
Hahnemann Medical College and Hospital of Philadelphia		(1940)
Laval University Faculty of Medicine		(1940)
University of Montreal Faculty of Medicine		(1940)
Medizinische Fakultät der Universität Wien		(1938)
Universität Bern Medizinische Fakultät		(1938)

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Vermont College of Medicine		(1925)	Vermont
McGill University Faculty of Medicine		(1927)	California

School	LICENSED BY ENDORSEMENT	Year Grad.
Tufts College Medical School		(1939)
Columbia University College of Physicians and Surgeons		(1937)
Karl-Franzens-Universität Medizinische Fakultät, Graz		(1923)
University of Edinburgh Faculty of Medicine		(1928)

North Carolina Reciprocity Report

The North Carolina Board of Medical Examiners reports 29 physicians licensed to practice medicine by reciprocity and 6 physicians so licensed by endorsement on June 16. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1930), (1938)	Arkansas
Yale University School of Medicine		(1937)	Michigan
University of Illinois College of Medicine		(1932)	Missouri
University of Louisville School of Medicine		(1938), (1940)	Kentucky
Tulane University of Louisiana School of Medicine		(1938)	Louisiana
Johns Hopkins University School of Medicine		(1922) (1930), (1933)	Tennessee, Maryland, (1932) Minnesota
University of Michigan Medical School		(1938)	Michigan
University of Buffalo School of Medicine		(1936)	New York
Univ. of Rochester School of Medicine and Dentistry		(1935)	New York
University of Oklahoma School of Medicine		(1930)	Oklahoma
Jefferson Medical College of Philadelphia		(1927), (1936)	Penna.
Temple University School of Medicine		(1933)	Penna.
Meharry Medical College		(1929), (1940)	Tennessee
University of Tennessee College of Medicine		(1936), (1939)	Tennessee
University of Texas Faculty of Medicine		(1933)	Texas
Medical College of Virginia		(1917), (1940)	Virginia
Univ. of Virginia Dept. of Medicine		(1926), (1933), (1937)	Virginia
University of Western Ontario Medical School		(1935)	New York

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Johns Hopkins University School of Medicine		(1936)	N. B. M. Ex.
Duke University School of Medicine		(1937) (1938), (1939, 3)	U.S.P.H.S., N. B. M. Ex.

Alabama Reciprocity Report

The Alabama State Board of Medical Examiners reports 13 physicians licensed to practice medicine by reciprocity and 2 physicians so licensed on endorsement of credentials of the National Board of Medical Examiners from May 1 through June 11. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1940)	Arkansas
Emory University School of Medicine		(1938)	Georgia
University of Illinois College of Medicine		(1937)	New York
Indiana University School of Medicine		(1921)	Indiana
State University of Iowa College of Medicine		(1932)	Iowa
Louisiana State University School of Medicine		(1940)	Louisiana
University of Michigan Medical School		(1925)	Michigan
Albany Medical College		(1931)	New York
Jefferson Medical College of Philadelphia		(1939)	N. Carolina
Temple University School of Medicine		(1937)	New Jersey
University of Pennsylvania School of Medicine		(1929) (1939)	New York, South Carolina
Baylor University College of Medicine		(1927)	Texas

School	LICENSED BY ENDORSEMENT	Year Grad.
Northwestern University Medical School		(1940)
Duke University School of Medicine		(1934)

New Mexico April Report

The New Mexico Board of Medical Examiners reports the written examination for medical licensure held at Santa Fe, April 14-15, 1941. The examination covered 12 subjects and included 100 questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. Eighteen physicians were licensed to practice medicine by reciprocity. The following schools were represented:

School	PASSED	Year Grad.
Yale University School of Medicine		(1930)
Northwestern University Medical School		(1941)

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1939, 2)	Arkansas
Northwestern University Medical School		(1906) (1929)	Wisconsin, Iowa
Rush Medical College		(1926)	Illinois
University of Illinois College of Medicine		(1930), (1936)	Illinois
State University of Iowa College of Medicine		(1933) (1936)	Iowa
Kansas Medical College, Medical Department of Washburn College		(1904)	Texas
New York Homeopathic Medical College and Hospital		(1894)	New York
Ohio State University College of Medicine		(1923)	Ohio
University of Oklahoma School of Medicine		(1938)	Oklahoma
Hahnemann Medical College and Hospital of Philadelphia		(1909)	Penna.
University of Pittsburgh School of Medicine		(1919)	Penna.
Vanderbilt University School of Medicine		(1936)	Tennessee
Baylor University College of Medicine		(1940)	Texas
Medical College of Virginia		(1915)	W. Virginia

Colorado June Report

The Colorado State Board of Medical Examiners reports the written examination for medical licensure held at Denver, June 10-12, 1941. The examination covered 8 subjects and included 68 questions. An average of 75 per cent was required to pass. Forty-one candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1941)*	81.5, 84.8, 87.3
University of Colorado School of Medicine		(1941)	81.8, 82, 82.3, 82.5, 83, 83, 83.3, 83.3, 84, 84.3, 84.3, 84.3, 84.3, 84.3, 84.8, 85, 85, 85, 85, 85.3, 85.5, 85.5, 85.8, 85.8, 86, 86, 86.3, 86.3, 86.3, 86.5, 87, 87, 87, 87.8, 88, 88, 88.3
University of Oklahoma School of Medicine		(1940)	86

* These applicants have completed four years' medical work and will receive the M.D. degree on completion of internship.

Maryland Homeopathic June Report

The Homeopathic Board of Medical Examiners of the State of Maryland reports the written examination for medical licensure held at Baltimore, June 24-25, 1941. The examination covered 9 subjects and included 70 questions. An average of 75 per cent was required to pass. Seven candidates were examined, all of whom passed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Hahnemann Medical Coll. and Hosp. of Philadelphia		(1940)	80, 84, 86, 88, 90, (1941) 80, 82

Oklahoma Reciprocity Report

The Oklahoma State Board of Medical Examiners reports 9 physicians licensed to practice medicine by reciprocity from January 16 through May 29. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Howard University College of Medicine		(1926)	Dist. Colum.
Tulane University of Louisiana School of Medicine		(1935)	Mississippi
Tufts College Medical School		(1935)	Mass.
St. Louis University School of Medicine		(1937)	Missouri
Washington University School of Medicine		(1935)	Missouri
Ohio State University College of Medicine		(1939)	Ohio
Western Reserve University School of Medicine		(1936)	Ohio
University of Texas School of Medicine		(1918)	Texas
University of Wisconsin Medical School		(1938)	Wyoming

Kansas June Report

The Kansas State Board of Medical Registration and Examination reports the written examination for medical licensure held at Kansas City, June 17-18, 1941. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Seventy-five candidates were examined, all of whom passed. Ten physicians were licensed to practice medicine by reciprocity and 1 physician so licensed on endorsement of credentials of the National Board of Medical Examiners. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Northwestern University Medical School		(1940) (1941)	83.1, 86.2
University of Kansas School of Medicine		(1941)	79.6, 79.7, 80.4, 80.7, 80.8, 81.7, 81.9, 81.9, 82.1, 82.2, 82.5, 82.5, 82.7, 82.9, 83, 83, 83.2, 83.2, 83.2, 83.3, 83.3, 83.7, 83.9, 84.1, 84.3, 84.3, 84.4, 84.5, 84.9, 85, 85.3, 85.5, 85.6, 85.8, 85.9, 86, 86.1, 86.1, 86.4, 86.6, 86.6, 86.7, 86.7, 87, 87.1, 87.6, 87.7, 87.7, 87.7, 88, 88.1, 88.1, 88.4, 88.5, 88.5, 88.6, 88.7, 89.1, 89.1, 89.2, 89.3, 89.6, 89.6, 90.6, 91.9, 92.6, 93
Tulane University of Louisiana School of Medicine		(1941)	82.9, 89.3
New York University College of Medicine		(1939)	88.1
University of Pennsylvania School of Medicine		(1941)	85.2, 87.2

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Northwestern University Medical School		(1937)	Illinois
Rush Medical College		(1938), (1939)	Illinois
Tufts College Medical School		(1915)	Nebraska
St. Louis University School of Medicine		(1937), (1939)	Missouri
Washington University School of Medicine		(1919), (1928), (1929), (1936)	Missouri

School	LICENSED BY ENDORSEMENT	Year Grad.
Yale University School of Medicine		(1936)

Ohio Reciprocity Report

The Ohio State Medical Board reports 18 physicians licensed to practice medicine by reciprocity and 3 physicians so licensed on endorsement of credentials of the National Board of Medical Examiners on April 1. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
College of Medical Evangelists		(1917)	California
University of Georgia School of Medicine		(1938)	Georgia
Northwestern University Medical School		(1936)	Wisconsin
Indiana University School of Medicine		(1936)	Indiana
Tulane University of Louisiana School of Medicine		(1931)	Texas
Johns Hopkins University School of Medicine		(1935)	Maryland, (1936) Michigan
University of Michigan Medical School		(1938), (1939)	Michigan
Detroit College of Medicine and Surgery		(1918)	Michigan
University of Minnesota Medical School		(1938)	Minnesota
St. Louis University School of Medicine		(1940)	Missouri
Washington University School of Medicine		(1931)	Missouri
University of Nebraska College of Medicine		(1931)	Nebraska
Columbia Univ. College of Physicians and Surgeons		(1935)	Minnesota
Hahnemann Medical College and Hospital of Phila.		(1929), (1936), (1939)	Pennsylvania

School	LICENSED BY ENDORSEMENT	Year Grad.
University of Colorado School of Medicine		(1934)
Northwestern University Medical School		(1938)
University of Rochester School of Medicine and Dentistry		(1938)

New York Endorsement Report

The New York State Board of Medical Examiners reports 109 physicians licensed to practice medicine by endorsement from January 18 through June 19. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Stanford University School of Medicine		(1931)	California
University of Southern California School of Medicine		(1938)	California
Yale University School of Medicine		(1933), (1934), (1938)	N. B. M. Ex.
Georgetown University School of Medicine		(1934)	Maryland, (1936) Penna., (1936), (1937), (1939) N. B. M. Ex.
Howard University College of Medicine		(1930)	Maryland
Emory University School of Medicine		(1926)	Georgia
Northwestern University Medical School		(1937)	Iowa, (1938) N. B. M. Ex.
The School of Medicine of the Division of the Biological Sciences		(1937)	Washington
State University of Iowa College of Medicine		(1928)	Iowa
Tulane University of Louisiana School of Medicine		(1922)	Alabama
Johns Hopkins University School of Medicine		(1934)	N. B. M. Ex. (1938, 2) Maryland
University of Maryland School of Medicine and College of Physicians and Surgeons		(1938, 2)	Maryland, (1939) N. B. M. Ex.
Boston University School of Medicine		(1938, 2), (1939)	N. B. M. Ex.
Harvard Medical School		(1932), (1934), (1936), (1937, 3), (1938, 2)	N. B. M. Ex., (1937) North Carolina
Tufts College Medical School		(1937), (1939)	N. B. M. Ex.
University of Michigan Medical School		(1925)	Michigan, (1933) N. B. M. Ex.
University of Minnesota Medical School		(1926)	Minnesota, (1940) N. B. M. Ex.
St. Louis University School of Medicine		(1939)	N. B. M. Ex.
Creighton University School of Medicine		(1939)	N. B. M. Ex.
University of Nebraska College of Medicine		(1934), (1935)	Nebraska, (1937) Oregon
Albany Medical College		(1937), (1939, 2)	N. B. M. Ex.
Columbia University College of Physicians and Surgeons		(1938, 3)	N. B. M. Ex.
Cornell University Medical College		(1935), (1939, 3)	N. B. M. Ex., (1938) Alabama
Long Island College of Medicine		(1938), (1939, 3)	N. B. M. Ex.
New York Medical College, Flower and Fifth Avenue Hospitals		(1938), (1939, 14)	N. B. M. Ex.
New York University College of Medicine		(1937), (1939)	N. B. M. Ex.
University of Buffalo School of Medicine		(1938), (1939, 4)	N. B. M. Ex.
Syracuse University College of Medicine		(1939)	N. B. M. Ex.
University of Rochester School of Medicine and Dentistry		(1937)	Virginia
Duke University School of Medicine		(1937), (1939)	N. B. M. Ex.
Western Reserve University School of Medicine		(1923)	N. B. M. Ex.
University of Oregon Medical School		(1936)	Washington
Hahnemann Medical College and Hospital of Philadelphia		(1936)	Penna.
Jefferson Medical College of Philadelphia		(1933)	Minnesota, (1935) West Virginia
Temple University School of Medicine		(1931), (1933)	Penna.
University of Pennsylvania School of Medicine		(1937)	Penna.
Woman's Medical College of Pennsylvania		(1938), (1939)	N. B. M. Ex.
University of Vermont College of Medicine		(1938), (1939, 2)	N. B. M. Ex.
University of Manitoba Faculty of Medicine		(1923)	Minnesota
University of Toronto Faculty of Medicine		(1932)	N. B. M. Ex.
University of Western Ontario Faculty of Medicine		(1930)	Ontario
McGill University Faculty of Medicine		(1939)	N. B. M. Ex.
Medizinische Fakultät der Universität Wien		(1924), (1934)	N. B. M. Ex.
Regia Università di Pisa Facoltà di Medicina e Chirurgia		(1936)	N. B. M. Ex.
Licentiate of the Royal College of Physicians, of the Royal College of Surgeons of Edinburgh and of the Royal Faculty of Physicians and Surgeons of Glasgow		(1939)	N. B. M. Ex.
American University of Beirut School of Medicine		(1940)	N. B. M. Ex.

Tennessee Endorsement Report

The Tennessee State Board of Medical Examiners reports 22 physicians licensed to practice medicine by endorsement from January 16 through May 28. The following schools were represented:

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1938)	N. B. M. Ex., (1940) California
Emory University School of Medicine		(1938)	N. Carolina
Rush Medical College		(1939)	Missouri
University of Illinois College of Medicine		(1939)	Illinois
University of Louisville Medical Department		(1903)	Kentucky
University of Louisville School of Medicine		(1940)	Kentucky
College of Physicians and Surgeons of Baltimore		(1906)	Virginia
University of Maryland School of Medicine and College of Physicians and Surgeons		(1929)	Ohio, (1937) Maryland
Washington University School of Medicine		(1937)	Missouri
University of Nebraska College of Medicine		(1935)	Nebraska
University of Buffalo School of Medicine		(1921)	New York
Jefferson Medical College of Philadelphia		(1930)	N. Carolina
University of Pennsylvania School of Medicine		(1933)	N. B. M. Ex.
University of Pittsburgh School of Medicine		(1930)	Penna.
Medical College of Virginia		(1915), (1928)	Virginia
Univ. of Virginia Department of Medicine		(1936), (1937)	Virginia
University of Manitoba Faculty of Medicine		(1937)	New Jersey
Queen's University Faculty of Medicine		(1918)	New Brunswick

Wyoming June Report

The Wyoming State Board of Medical Examiners reports the written examination for medical licensure held at Cheyenne, June 2-3, 1941. The examination covered 12 subjects and included 89 questions. An average of 75 per cent was required to pass. Three candidates were examined and passed. Seven physicians were licensed to practice medicine by endorsement. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
College of Medical Evangelists		(1941)	82
University of Colorado School of Medicine		(1940)	81
Loyola University School of Medicine		(1941)	84*

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Colorado School of Medicine		(1938)	Colorado
University of Georgia School of Medicine		(1929)	Georgia
University of Nebraska College of Medicine		(1914), (1932)	Nebraska
University and Bellevue Hospital Medical College		(1916)	Connecticut
Syracuse University College of Medicine		(1936)	Illinois
University of Alberta Faculty of Medicine		(1940)	Canada

* License has not been issued.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Autopsy: Liability of Coroner for Ordering Unauthorized Autopsy.—Apparently in the course of his employment Crenshaw collapsed and was taken to the nearby office of a cult practitioner who pronounced him dead and notified the defendant, the county coroner. On the direction of the coroner an undertaker then removed the body to the county hospital. Without ordering an inquest, without making any investigation whatever other than having a telephone conversation with the cult practitioner referred to, in which the coroner was informed that Crenshaw had "reportedly fallen over dead while working," and without himself examining the body, the coroner ordered an autopsy to be performed by the department of pathology of a local medical school. The autopsy was performed without the consent of Crenshaw's widow, who did not learn of it until some time after burial. Subsequently she sued the coroner. The jury returned a verdict for $5,000 for actual damages and for $5,000 for punitive damages. The trial court ordered a remittitur of the whole amount of the punitive damages awarded and entered judgment for the total amount awarded for actual damages. The coroner then appealed to the St. Louis court of appeals, Missouri.

The coroner in Missouri, said the court of appeals, is a constitutional officer whose powers and duties with respect to the holding of inquests and autopsies are more or less specifically defined and limited by statute. In the opinion of the court, the decision of the Kansas City court of appeals in *Patrick* v. *Employers Mutual Liability Insurance Co.*, 233 Mo. App. 251,

118 S. W. (2d) 116 (J. A. M. A. **112**:2466 [June 10] 1939), in which the Missouri statutes relating to coroners were construed, was determinative on the issues presented in the present case. In the Patrick case, said the court of appeals, it was held squarely that a coroner is invested by law with no authority to order an autopsy performed except in connection with, and as an incident to, an inquest to be held before a jury on the body of a person supposed to have come to his death by violence or casualty. In the Patrick case the court held that the purpose of an inquest was to inquire, on a view of the body, how and by whom such person came to his death; that, while the coroner acts judicially and has a discretion with respect to determining whether an inquest shall be held, neither the inquest itself nor the calling and holding of an autopsy in connection with it is a proceeding judicial in character so as to relieve the coroner from civil liability for his acts in relation to it; that it was never intended that the coroner should have the right to order an autopsy performed in any case in which, in his mere judgment, an autopsy might be deemed proper for any such reason as the advancement of science or the like, and that while it might or might not be thought desirable that the coroner should have the power to hold an autopsy to determine whether an inquest should be held the law gives him no such authority, so that in the case of a person who is merely supposed to have come to his death by violence or casualty an autopsy performed except in connection with an inquest is unlawful and illegal, regardless of what might be the coroner's good faith in the exercise of a mistaken authority in the matter. Of course, continued the St. Louis court, if the widow, as the person entitled to the right of sepulture, had given her consent to the autopsy, there would have been no liability on the coroner's part (in the absence of a performance of the autopsy in an improper manner), even though no inquest was held or basis afforded for the defendant himself to have declared the cause of death on a mere coroner's view of the body. However, neither the widow nor any one for her gave such consent, and consequently the autopsy must be held to have been unlawful and illegally performed.

The coroner contended that he was justified in ordering an autopsy to enable him to sign a death certificate. The answer to this, said the court, is the fact that, under the statute having to do with the coroner's duties with respect to the registration of deaths, he is authorized to execute a certificate of death only if the case is referred to him by the local registrar of vital statistics because of the absence of an attending physician and because the circumstances of the death render it probable that the death was caused by unlawful or suspicious means. In this case, not only was the deceased receiving treatment from a physician for high blood pressure up to the very time of his death but in addition the case was concededly not referred to the defendant by the registrar for investigation and certification. Neither was the defendant requested by the relatives or friends of the deceased to hold a view or inquest on the body for the purpose of issuing a certificate of the cause of death. In the opinion of the court, the autopsy performed on the body was not to be justified on any such ground.

The coroner next contended that the trial court erred in refusing to permit the physician who performed the autopsy to answer a question put to him on cross examination as to whether the cause of death could have been ascertained without an autopsy on the ground that the question at issue was not whether the cause of death could have been ascertained without an autopsy but whether the defendant had in any event possessed the legal right to direct the performance of the autopsy. However effective, said the court of appeals, an autopsy might have been as a means of revealing the true cause of death, such a consideration would not have excused its performance without legal authority therefor, and, in the absence of such authority, the matter of its desirability was irrelevant to the case unless, perhaps, on the question of the coroner's good faith.

The court of appeals believed an award for actual damages for the unlawful performance of an autopsy was proper even though the only damages sustained by the widow were for mental anguish. While ordinarily damages for mental anguish are not recoverable unless connected with some physical injury, the trend of modern authority is not to apply such a restriction in the case of interference with rights involving dead bodies, where mental anguish to the surviving relatives is not only the natural and probable consequence of the character of the wrong committed but indeed is frequently the only injurious consequence to follow. The court believed, however, that the amount awarded for actual damages was excessive under the circumstances here present. The autopsy in this case was performed in a proper and scientific manner. There was no mutilation of the body visible to the eye. While the widow undoubtedly suffered mental anguish in more or less degree from the mere knowledge that even a proper autopsy had been performed, a state of grief on her part was none the less a natural consequence of the death of her husband in and of itself, and there was nothing to show that the reaction of which she complained was materially different from that which would have followed in any event if there had been no autopsy performed on the body. The court then adverted to the amount awarded for actual damages in the Patrick case—$1,500—and felt that that sum furnished an accurate guide beyond which the limits of reasonable compensation for actual damages should not be permitted to extend in the absence of special and unusual circumstances. Accordingly the court, in effect, ordered a judgment for $1,500 in favor of the widow.—*Crenshaw v. O'Connell, 150 S. W. (2d) 489 (Mo., 1941).*

Society Proceedings

COMING MEETINGS

American Academy of Pediatrics, Boston, Oct. 8-11. Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill., Secretary.

American Association for the Study of Neoplastic Diseases, Washington, D. C., Sept. 4-6. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 11-13. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Association of Railway Surgeons, Chicago, Sept. 8-10. Dr. Daniel B. Moss, 547 West Jackson Blvd., Chicago, Secretary.

American Clinical and Climatological Association, Skytop, Pa., Oct. 16-18. Dr. Francis M. Rackemann, 263 Beacon St., Boston, Secretary.

American Congress of Physical Therapy, Washington, D. C., Sept. 1-5. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

American Hospital Association, Atlantic City, N. J., Sept. 15-19. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.

American Public Health Association, Atlantic City, N. J., Oct. 14-17. Dr. Reginald M. Atwater, 50 West 50th St., New York, Executive Secretary.

American Roentgen Ray Society, Cincinnati, Sept. 23-26. Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal, Canada, Secretary.

Central Association of Obstetricians and Gynecologists, New Orleans, Oct. 2-4. Dr. William F. Mengert, 515 Newton Road, Iowa City, Secretary.

Colorado State Medical Society, Estes Park, Sept. 17-20. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.

District of Columbia, Medical Society of the, Washington, Sept. 30-Oct. 2. Mr. Theodore Wiprud, 1718 M Street N.W., Washington, Secretary.

Indiana State Medical Association, Indianapolis, Sept. 23-25. Mr. Thomas A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

Kentucky State Medical Association, Louisville, Sept. 29-Oct. 3. Dr. Arthur T. McCormack, 620 South Third St., Louisville, Secretary.

Michigan State Medical Society, Grand Rapids, Sept. 16-18. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing, Secretary.

Mississippi Valley Medical Society, Cedar Rapids, Iowa, Oct. 1-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

Nevada State Medical Association, Elko, Sept. 26-27. Dr. Horace J. Brown, P. O. Box 698, Reno, Secretary.

Oregon State Medical Society, Portland, Sept. 3-6. Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Secretary.

Pacific Association of Railway Surgeons, Salt Lake City, Sept. 12-13. Dr. W. T. Cummins, 1400 Fell St., San Francisco, Secretary.

Pennsylvania, Medical Society of the State of, Pittsburgh, Oct. 6-9. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Rocky Mountain Medical Conference, Yellowstone Park, Wyo., Sept. 2-4. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver, Secretary.

Vermont State Medical Society, Burlington, Oct. 2-3. Dr. Benjamin F. Cook, 154 Bellevue Ave., Rutland, Secretary.

Virginia, Medical Society of, Virginia Beach, Oct. 6-8. Miss A. V. Edwards, 1200 East Clay St., Richmond, Secretary.

Washington State Medical Association, Seattle, Aug. 24-26. Dr. Vernon W. Spickard, 1305 Fourth Ave., Seattle, Secretary.

Wisconsin, State Medical Society of, Madison, Sept. 10-12. Mr. G. B. Larson, 110 East Main St., Madison, Assistant Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1931 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Hygiene, Baltimore

33:65-94 Section A (May) 1941. **Partial Index**

69-100 Section B 69-112 Section C 71-112 Section D

Section B

Pathology of Equine Encephalomyelitis in Young Chickens. E. E. Tyzzer and A. W. Sellards, Boston.—p. 69.

Fermentative Variability and Serologic Identity of Organisms Isolated from Food Poisoning Outbreak. Elinor Van Dorn Smith, Northampton, Mass.—p. 82.

Antigenic Properties and Tissue Specificity of Broths as Shown by Precipitation, Complement Fixation and Anaphylaxis. G. H. Bailey and S. Raffel, Baltimore.—p. 86.

Section C

Summary of "Tarsimaculatus" Complex of Anopheles (Diptera: Culicidae). L. E. Rozeboom and A. Gabaldon, Baltimore.—p. 88.

New Drug Effective Against Bird Malaria. R. Hegner, Evaline West, Mary Ray and Marian Dobler, Baltimore.—p. 101.

Section D

Studies on Acquired Immunity to Dwarf Tapeworm, Hymenolepis Nana Var. Fraterna, in Mouse Host. J. T. Hearin, Baltimore. —p. 71.

Studies on Oxyuriasis: XXIII. Survival of Eggs of Enterobius Vermicularis Under Known Conditions of Temperature and Humidity. Myrna F. Jones and L. Jacobs, Washington, D. C.—p. 88.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

45:641-800 (May) 1941. **Partial Index**

Radiosensitivity of Tumors. S. Warren, Boston.—p. 641.

*Comments on Treatment and Sequelae of Carcinoma of Uterus. Elizabeth Newcomer, Denver.—p. 651.

*Failures Following Treatment by Irradiation of Cases of Benign Uterine Bleeding and Fibromyoma. J. A. Corscaden, New York.—p. 661.

Effects of Roentgen Irradiation on Experimental Hyperthyroidism. L. H. Garland, W. C. Cutting, G. B. Robson and W. W. Newman, San Francisco.—p. 692.

Radiodermatitis Among Physicians. E. T. Leddy and F. J. Rigos, Rochester, Minn.—p. 696.

Primary Tumors of Lungs: Roentgen Diagnosis and Therapy; Report of 130 Cases. B. E. Farberov and E. A. Baslow, Kharkov, Soviet Union.—p. 701.

Progressive Hepatolenticular Degeneration with Electroencephalograms and Pneumoencephalograms: Report of Case. H. Weatherly, Boston. —p. 714.

Roentgen Ray Aid in Diagnosis of Acute Portal Thrombosis (Pylephlebitis). A. Bassler, New York.—p. 724.

Unusual Locking of Elbow Joint by Sesamum Cubiti and Free Joint Body. M. S. Burman, New York.—p. 731.

Radiology in the United States Army. W. W. McCaw, Ancon, Canal Zone.—p. 733.

Explosion and Fire Hazard of Anesthetics in Presence of Roentgenologic Apparatus. B. A. Greene, Brooklyn.—p. 737.

Biophotometric Measurements of Dark Adaptation Among Roentgenologists: Measure of Vitamin A Deficiency. H. H. Lerner, Boston.—p. 753.

Carcinoma of Uterus.—According to Newcomer, fistulas are seldom due to faulty methods of irradiation but to the extension of the disease. Constriction of the ureters, ureteral dilatation and hydronephrosis are also generally due to extension. A dull, nagging pain in the hips, groin or radiating down the thigh or leg may be caused by ureteral obstruction. Cystoscopy and visualization of the ureters are indicated in such cases. Similar symptoms are caused by extension of the disease to the lumbar and sacral nerves and to the uterosacral ligaments. Masses may form on the side walls of the pelvis by extension through the parametrium and broad ligaments, causing excruciating pain. Pressure on the veins of the lower extremities may result in edema of the lower limbs and external genitalia. Invasion of the rectum may result in stenosis, ulceration, intestinal obstruction and fistulas. If low abdominal pain follows radium application, patency of the cervical canal must be established. Cancerous tissue may be growing upward along the ureters behind the peritoneum with consequent involvement of the abdominal organs and the peritoneum. The disease rarely spreads through the abdominal and thoracic nodes to the supraclavicular regions. Metastasis to the bones does not occur as often in uterine cancer as in other forms of cancer. Roentgen therapy should precede radium therapy. It reduces infection and the size of the tumor, makes the application of radium safer, renders possible the giving of a heavier dose of radium and distributes it more evenly throughout the tumor. It makes unnecessary the giving of radium in divided doses, except in an extremely large uterus. Radium should be given in both the uterine and the cervical canals in doses short of tolerance by the surrounding tissues. As large a dose of radium as can be safely tolerated should be applied to the vault of the vagina by means of the bomb, colpostat or interstitial irradiation in selected cases. Roentgen therapy, by means of at least 300 kilovolts, should be evenly distributed throughout the true pelvis. The treatment is repeated in six weeks. The addition of two lateral fields and another field over the lumbar vertebrae would minimize extensions to the side walls of the pelvis and to the lumbar area, which are especially subject to extensions. The author's method is to cauterize the area from which a biopsy specimen has been taken. Roentgen treatment is then given every other day to two pelvic ports, anterior and posterior, each 20 cm. square. An average size patient receives 1,300 roentgens over each port in fourteen days. Within four to seven days radium is applied. Usually 100 mg. is distributed in 5 mg. needles. The radium usually remains in place for thirty-six hours. Three or four days later a vaginal bomb containing 100 mg. of radium is placed in the vaginal canal against the cervix for from twenty-four to thirty-six hours.

Benign Uterine Bleeding and Fibromyoma.—In Corscaden's experience bleeding was controlled in 98.1 per cent of the 733 cases of uterine bleeding and myoma treated with radium and roentgen irradiation. Thirty (6.1 per cent) of 493 patients treated by radium and 18 (7.6 per cent) of 240 treated by roentgen irradiation required supplementary irradiation. Fourteen (1.9 per cent) of the 733 patients failed to have the bleeding controlled. Five of these received inadequate doses of radium or roentgen rays, 4 were operated on before sufficient time had elapsed for the irradiation to complete its effect and 2 had pedunculated submucous myoma. Three failures were unexplained. Dysmenorrhea disappears when menstruation ceases. Following substerilizing doses this symptom reappears in 66 per cent of the patients in whom menstruation returns. Pain other than dysmenorrhea and urinary symptoms have been relieved in less than 50 per cent. Uterine tumor is satisfactorily reduced in 94 per cent of patients if it is no larger than a pregnancy of five months. When larger than a pregnancy of six months, it has been satisfactorily reduced in only 40 per cent. Following a substerilizing dose of radiation, in only 2 of 15 fibromyomas was the tumor satisfactorily reduced while menstruation still continued. Two patients had symptoms and signs of tumor degeneration following roentgen therapy. In no instance has roentgen therapy caused a pelvic inflammation to flare up. Four patients treated with radium contracted surgical infection following dilation and curettage and the insertion of radium into the uterus. No instance of carcinoma of the uterus has been revealed within two years after radium and roentgen therapy for benign bleeding or myoma. Two cystadenomas of the ovary were discovered four and five years, respectively, after irradiation. The 733 cases were a carefully selected group and represented about 30 per cent of the total number of such cases encountered. The others were curable by conservative methods or presented conditions which contraindicated radium or roentgen therapy. Of the contraindications only the submucous myoma is important as a cause of failure to control bleeding, and carcinoma of the uterus and a neoplasm of the ovary a cause of disaster from neglect.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

25:265-396 (May) 1941

Case Control Methods in Dispensary Gonorrhea. R. Deakin and M. S. Wortman, St. Louis.—p. 265.
Value of Tabulating Unit to Gonorrhea Clinic. D. K. Hibbs and B. H. Dickerson, Chicago.—p. 270.
Effect of Syphilis and Its Treatment on Incidence of Toxemia of Pregnancy. C. H. Peckham, Baltimore.—p. 280.
Supposed Detoxifying Effect of Various Substances Used in Association with Arsphenamines. G. O. Doak, Baltimore.—p. 286.
Studies on Role of Spirochaeta Pallida in Wassermann Reaction: I. Complement Fixation in Syphilis, Leprosy and Malaria with Spirochetal Antigens. J. A. Kolmer, Clara C. Kast and Elsa R. Lynch, Philadelphia.—p. 300.
Rapid Slide Flocculation Test for Syphilis. F. Márquez, Rosita, Coahuila, Mexico.—p. 319.
Effect of Sulfanilamide and Related Compounds on Gonococcus and Experimental Gonococcic Infection in Mice. A. Cohn, New York. —p. 324.
*Further Observations on Gonococcic Vulvovaginitis. A. Cohn, A. Steer and Eleanor L. Adler, New York.—p. 329.
*Studies of Transmissibility of Syphilis: Infectiousness of Vaginal Secretions and Menstrual Blood of Syphilitic Women. H. Pariser, Philadelphia.—p. 339.

Gonococcic Vulvovaginitis.—Cohn and his associates made a twenty-eight week follow-up study on 234 cases of gonococcic vulvovaginitis. The superiority of cultures over smears for diagnosis and for determining cure was evident. As the length of observation increases and the disease progresses, or if treatment is instituted, the accuracy of diagnosis by the smear method decreases. Toward the end of the twenty-eight weeks of observation there are few instances of positive diagnosis by either smear or culture. At this time, because some children probably have been reinfected, there is a greater degree of correspondence between smear and culture. Of a total of 1,070 examinations 98.9 per cent were positive by culture and 67.1 per cent by smear. It was found that more than 50 per cent of untreated patients undergo spontaneous cure within thirteen weeks. The carrier state develops in about one fifth of these patients, in whom occasional positive cultures occur in the absence of clinical signs even after twenty-eight weeks of observation. However, all patients ultimately become negative. Sulfanilamide therapy resulted in cure in two thirds of the hospitalized patients within two weeks of treatment. Sulfapyridine was followed promptly by negative cultures in all cases, with recurrence in less than 10 per cent. Estrogen brought about early clinical improvement, but the course of the disease was little different from that in the untreated controls. Rectal cultures were positive in 45 per cent of the patients. In none was there characteristic evidence of gonococcic proctitis clinically.

Transmissibility of Syphilis.—In determining the transmissibility of syphilis, Pariser injected vaginal secretions from 30 untreated syphilitic women under the dorsal skin of mice. The vaginal secretions from 7 women produced syphilis in animals. Five of these 7 women had local cervical lesions. The clinical manifestations of the disease in these instances varied from about one week to six and one-half years. The sixth "positive" result was obtained from the menstrual blood of a secondary syphilitic woman with no local cervicovaginal lesions, and the seventh was produced from an early secondary syphilitic pregnant woman whose cervix was edematous, bluish and boggy, but who presented no visible open lesions. Initial darkfield examination revealed organisms in small numbers closely conforming to the universally accepted morphology of Spirochaeta pallida in 4 cases and organisms which were slightly thicker than average but which by subsequent animal inoculation were proved to be Spirochaeta pallida in 2 instances; the result was negative in the seventh case. In the absence of lesions the darkfield examination of 50 per cent of the women revealed spirochetes easily distinguished from Spirochaeta pallida unless wide latitude is permitted in the interpretation of the spirochetal form of the organism of syphilis. The case material consisted of 76 per cent early (within the first four years of the disease) syphilis and 24 per cent late syphilis. The conclusions from the study that the syphilitic woman discharges spirochetes into the vagina only in the presence of local lesions or through her menstrual blood during the early stages are not to refute the point of view that syphilis may be acquired without the production of a lesion or that the woman may temporarily before or after acquiring the disease harbor the spirochetes on the presumably intact cervix. The conclusions do postulate, however, that, once infection has been acquired, the woman whose biologic reaction is thereby considerably altered to the organism discharges Spirochaeta pallida into the vagina only in the presence of lesions which may occur early or chronologically late when the immunity balance shifts toward the development of infectious, relapsing, even though at times inconspicuous and transient lesions. Among the 23 patients the infectiousness of whose vaginal secretions could not be demonstrated there were 5 (4 early and 1 late) from whom two or three vaginal washings were collected on different days to detect any possible changes in the pathogenicity of the flora over one or two weeks. The results were "negative." Their vaginal secretions varied from mucoid to purulent. In 2 instances primary inoculation of vaginal secretions into mice killed the animals within a week.

American Review of Tuberculosis, New York

43:581-712 (May) 1941

*BCG Vaccination in Montreal: Statistical Analysis of Results of Research by Dr. J. A. Baudouin on BCG Vaccination in Montreal. J. W. Hopkins, Ottawa, Ont., Canada.—p. 581.
*Pulmonary Tuberculosis in Medical Students and Nurses. R. G. Hahn, C. Muschenheim and J. Freund, New York.—p. 600
Lymphohematogenous Tuberculosis. S. Cohen, Jersey City, N. J. —p. 612.
Gastrointestinal Complications in Pulmonary Tuberculosis. L. L. Hardt and S. J. Cohen, Chicago.—p. 628.
Tuberculosis in Rat: III. Correlation Between Histologic Changes and Fate of Living Tubercle Bacilli in Organs of Albino Rat. C. C. Wessels, Philadelphia.—p. 637.
Tuberculosis of Tonsils and Skin: Contribution to Theory of Origin of Langhans' Giant Cells. S. Tannhauser, Tucson, Ariz.—p. 663.
Meinicke Flocculation Reaction for Tuberculosis. W. H. McMenemey, Oxford, England.—p. 670.
Leukocytes in Tuberculosis: Further Test of Validity of Pathologic Interpretation of Leukocytic Counts in Tuberculous Patients. E. M. Medlar, New York.—p. 680.
The Law of Small Numbers, as Applied to Virulence Measurement. W. N. Berg, New York.—p. 685.
Dermatopulmonary Reaction: I. Behavior of Dermatopulmonary Reaction in Artificial Pneumothorax. S. Puder, Budapest, Hungary.—p. 692.
Id.: II. Changes in Nervous System Associated with Dermatopulmonary Reaction. S. Puder, Budapest, Hungary.—p. 699.
Id.: III. Influence of Dermatopulmonary Reaction on Experimental Miliary Tuberculosis. S. Puder, Budapest, Hungary.—p. 709.

BCG Vaccination.—Hopkins states that more than 20,000 Montreal infants were given BCG vaccine on the advice of physicians and with the consent of parents. His study is limited to 793 of these children who were exposed to contact with a patient having positive sputum and to approximately 1,200 control children in similar contact not given the vaccine. The children of both groups were drawn from the lower middle and poorer sections of the community. Of 30 deaths from causes other than tuberculosis among the vaccinated children, 4 were confirmed at necropsy and 11 by clinical and laboratory examinations. There were 37 deaths from nontuberculous causes among the control group; 2 of these were confirmed at necropsy and 15 by hospital examination. There were 8 deaths from tuberculosis among the vaccinated group, 3 confirmed at necropsy, 3 by hospital examination and 1 by a specialist in tuberculosis. The remaining child who died was diagnosed clinically as having pulmonary and meningeal tuberculosis, and both parents had active pulmonary tuberculosis. Of the 23 tuberculosis deaths among the control group, 1 was confirmed at necropsy, 10 by hospital examination and 3 by specialists. As to tuberculosis morbidity, there were 37 active and latent morbid cases in the vaccinated group; 32 diagnoses were confirmed by roentgen or fluoroscopic examination and 32 by hospital observation. Among the control group there were 81 active or latent instances of tuberculosis; 71 were confirmed by roentgen or fluoroscopic examination and 77 by hospital observation. With but two exceptions (at the age of 4 and 5) the differences in the general mortality by age of both groups are in favor of the vaccinated children. Even the combined rate for the age groups from 0 to 4 years of age of controls differs from the vaccinated rate of 86 by only 1.8 times its standard error. The morbidity figures favor the vaccinated children. Analysis shows that the oral administration of BCG vaccine at birth substantially reduced the incidence of tuberculosis during the third, fourth and fifth

years of life and that, had larger numbers been available for comparison, there probably would have been significant reductions in the first two years of life. As the vaccinated children were exposed to a slightly higher accumulated duration of contact and were of a lower average age at the beginning of contact, it seems reasonable to ascribe the favorable differences in their "pathologic infection" to the effects of vaccination. The similarity of the vaccinated and control groups in respect to nontuberculosis mortality is not indicative of any pronounced paraspecific immunity resulting from BCG, as has been suggested by some investigators. Acceptable information regarding the duration of the effectiveness of vaccination may be secured only by continued observation of the children now in the lower age groups.

Pulmonary Tuberculosis in Medical Students and Nurses.—Hahn and his associates report the results of tuberculosis case finding (by the intracutaneous tuberculin test and roentgenogram of the chest) among medical and nurse students at Cornell University Medical College and the New York Hospital. The percentage of positive reactors among six first year classes of medical students varied from 75 to 89. Collectively, of the 315 tested 259, or 82.2 per cent, were positive and 56, or 17.7 per cent, were negative. Of three fourth year classes totaling 147 students, 135, or 91.8 per cent, were positive and 12, or 8.1 per cent, were negative. The percentage of positive reactors in the fourth year classes tested was thus 9.6 higher than in the first year classes. Of the total of 278 student nurses of the classes of 1935 to 1941, inclusive, tested in their first year 216, or 77.6 per cent, were positive and 62, or 22.3 per cent, were negative. Of the classes of 1934 and 1936, totaling 69 nurses, examined during their second year 57, or 82.6 per cent, were positive and 12, or 17.4 per cent, were negative. The classes of 1933, 1935, 1936, 1937 and 1938 were examined at the end of their third year, and of 130 graduating nurses tested 119, or 91.5 per cent, were positive and 11, or 8.5 per cent, were negative. The student nurses thus showed an increase of positive reactors from 77.6 per cent the first year to 91.5 per cent at graduation. The percentage of negative reactors shortly before graduation of both medical and nursing student groups varied in different years from 0 to 14.3. The average for the nursing students (of the classes of 1933 to 1939 inclusive) has been 6 per cent negative on graduation and for the medical students 8.7 per cent. A total of 442 medical students had at least one roentgen examination; 71, or 16.1 per cent, had calcified deposits in the tracheobronchial lymph nodes, in the pulmonary parenchyma or in both, and 5 had shadows characteristic of chronic pulmonary tuberculosis in their initial roentgenograms. The lesions were all minimal in extent. Only 2 of the 5 were found in the first academic year. Four other students, who had negative initial roentgenograms, had characteristic shadows of chronic pulmonary tuberculosis in subsequent years. Three were minimal and 1 was moderately advanced. Of these 9 students, 2 per cent of the total, 4 had lesions which were obviously progressive and they were referred to sanatoriums. The other 5 were allowed to complete their course. Of these, subsequent information is available on 2; 1 has never had any symptoms or physical signs attributable to his lesion, which has remained unchanged in serial roentgenograms for four years and the disease of 1 has progressed since his graduation. Roentgenograms of the chest of 269 nurses were obtained and 52, or 19.3 per cent, had calcified nodules and 14, or 5.2 per cent, had doubtful apical shadows of not more than a few millimeters. In none of these did definite pulmonary infiltrations develop during the period of observation. Three nurses were found to have definite pulmonary lesions of the so-called adult type. They were all in the minimal stage when discovered; 2 of them were observed in the initial roentgenogram; thus the disease developed in only 1 of the 269 student nurses during their three years of training. The rates for the nurses and the medical students are considerably below those reported from similar institutions. The tuberculosis rate among the medical students, though slightly higher than that among the student nurses, is not significantly higher than the expected rate for their age group (average 22 years on admission).

Archives of Pathology, Chicago

31:665-840 (June) 1941

Histology of Human Yellow Fever When Death Is Delayed. E. Villela, Rio de Janeiro, Brazil, South America.—p. 665.

Absorption of Liquid Petrolatum ("Mineral Oil") from Intestine: Histologic and Chemical Study. W. A. Stryker, Chicago.—p. 670.

Synovial Membrane in Charcot's Joint, with Special Reference to Golgi Apparatus and Synovial Fluid. E. S. J. King, Melbourne, Australia. —p. 693.

Spontaneous Fibromyoma in Female Guinea Pig. A. Lipschütz, Santiago, Chile, South America.—p. 702.

Relation of Vitamin E to Effectiveness of Testosterone Injected into Caponized Male Fowls. F. B. Adamstone, Urbana, Ill.—p. 706.

Cholesterol Content of Brain in Nutritional Encephalomalacia of Vitamin E-Deficient Chicks. F. B. Adamstone, Urbana, Ill.—p. 711.

Reticulum Cell Sarcoma Following Ulceration of Intestine in Vitamin E-Deficient Chicks. F. B. Adamstone, Urbana, Ill.—p. 717.

Relation of Vitamin E to Substances of Anthracene Group. F. B. Adamstone, Urbana, Ill.—p. 722.

Pigmented Villonodular Synovitis, Bursitis and Tenosynovitis. H. L. Jaffe, L. Lichtenstein and C. J. Sutro, New York.—p. 731.

Histologic Distribution of Vitamin A in Human Organs Under Normal and Under Pathologic Conditions. H. Popper, Chicago.—p. 766.

Archives of Physical Therapy, Chicago

22:261-314 (May) 1941

Physiologic Implications of Physical Therapy. J. L. Halliday, Glasgow, Scotland,—p. 261.

Effect of Short Wave Diathermy on Arterial Pressures: Experimental Study. R. L. Bennett, E. C. Elkins and J. F. Herrick, Rochester, Minn.—p. 266.

Short Wave Diathermy in Treatment of Gingivitis. D. Kobak, Chicago. —p. 282.

*Symptomatic Relief in Chronic and Acute Arthritides by Histamine Iontophoresis. R. E. Reiley and M. E. Knapp, Minneapolis.—p. 288.

Histamine Iontophoresis for Arthritis.—Reiley and Knapp used histamine iontophoresis in the treatment of 40 ambulatory patients with arthritis. Complete relief was obtained by 23 patients, 12 experienced partial relief and 5 obtained no benefit.

Archives of Surgery, Chicago

42:969-1108 (June) 1941

Destruction of Prothrombin and Storage of Vitamin K. J. G. Allen and C. Vermeulen, Chicago.—p. 969.

Hydatid Cyst of Liver. J. Arce, Buenos Aires, Argentina, South America.—p. 973.

*Progressive Postoperative Gangrene of Skin. H. Dodd, J. W. Heekes and H. Geiser, London, England.—p. 988.

*Metastasis of Primary Carcinoma of Breast, with Special Reference to Spleen, Adrenal Glands and Ovaries. O. Saphir and M. L. Parker, Chicago.—p. 1003.

Effects of Uncomplicated Hemoconcentration (Erythrocytosis), with Particular Reference to Shock. G. O. Wood, Rochester, Minn., and A. Blalock, Nashville, Tenn.—p. 1019.

Results of Removal of Acoustic Tumors by Unilateral Approach. W. E. Dandy, Baltimore.—p. 1026.

Visualization of Pulmonary Artery During Its Embolic Obstruction. J. H. Jesser and G. de Takáts, Chicago.—p. 1034.

Traumatic Vasospastic Dystrophy of Extremities. L. N. Atlas, Cleveland.—p. 1042.

X. The Inadequately Treated Cretin. I. P. Bronstein and W. H. Reals, Chicago.—p. 1048.

Comparison of Effects of Heat and Those of Cold in Prevention and Treatment of Shock. A. Blalock and M. F. Mason, Nashville, Tenn. —p. 1054.

Pelvic Actinomycosis. J. A. Tuta, Chicago.—p. 1060.

Basis and Treatment of Calcification of Tendinocapsular Tissues, Especially Supraspinatus Tendon. C. J. Sutro and L. J. Cohen, New York.—p. 1065.

*Renal Blood Flow and Sympathectomy in Hypertension. A. C. Corcoran and I. H. Page, Indianapolis.—p. 1072.

New Method for Physiologic Decompression After Gastric Operations: Preliminary Report. W. Raffel, Baltimore.—p. 1083.

*Early Rising and Ambulatory Activity After Operation a Means of Preventing Complications. D. J. Leithauser and H. L. Bergo, Detroit. —p. 1086.

Carcinoma of Cystic Duct: Report of Case and Comments on Ligation of Hepatic Artery in Man. A. Brunschwig and D. E. Clark, Chicago. —p. 1094.

Postoperative Gangrene of Skin.—Three cases of progressive postoperative gangrene of the skin reported by Dodd and his co-workers were the first to be seen in an active surgical experience of thirty years. The gangrene of 1 occurred after a suprapubic prostatectomy. Stewart-Wallace collected 37 cases in the period from 1908 to 1935; since then about 40 new cases have been reported, making a total of 87. In 71 cases gangrene developed after abdominal and thoracic visceral operations, and in 16 it followed minor parietal lesions. All of the lesions, with two exceptions (herniotomy and sympathectomy), were primarily due to mixed or single infections. There was a striking

predominance of male over female patients among the visceral group, the proportion being 53 to 17. The parietal lesions were distributed equally. The authors suggest that the male predominance is probably due to the fact that the skin of the male trunk is thicker, coarser and more hairy than that of the female. Thus, staphylococci are inevitably in the hair follicles and virulent streptococci can be introduced into the skin with a needle. Most of the patients (69 of 86) were more than 35 years of age, indicating that progressive postoperative gangrene of the skin is associated with declining vitality. General debility may therefore be a significant etiologic factor. In the 61 in which these data were available the gangrene was generally present within three weeks after operation. All treatment, except with the cautery, is useless. Of 22 fatalities the cautery was used in 8, while of 65 recoveries the wound was cauterized in 52. Two other methods of treatment have emerged; the use of maggots and excision by scalpel. Coakley and Klein succeeded in clearing up with maggots a condition which had persisted in spite of electrosurgical excision. Holman tried this therapy in 3 cases; in 1 the maggots would not stay in the wound and the patient died, and the 2 other patients recovered. Willard had success with a case of gangrene following appendectomy in which the entire lower abdominal wall was involved. He excised the area, the sloughs and the spreading edge in the skin with a scalpel, afterward dressing it daily with a watery suspension of zinc peroxide. Recovery is possible even after the gangrene has existed six months. Thirteen of the 22 patients died within three to nine months after the onset of the disease. Nineteen of the deaths occurred among the 69 patients who were 35 or more years of age. The death rate for visceral lesions was 24.3 per cent, as compared to 31.2 per cent for parietal conditions.

Metastasis from Carcinoma of Breast.—Saphir and Parker found the adrenals, ovaries and spleen to be involved in a surprisingly large percentage of the 43 necropsies on patients with carcinoma of the breast. The most common locations were the lungs (28 instances) and the liver (24 instances), while the next most common locations were the adrenals in 19 instances, the spleen in 10 and the ovaries in 7. These figures when compared with those of older publications are exceptionally high. No metastases were found in 3 instances. It is definitely not the type of carcinoma which is responsible for the shorter or longer survival period of the patient or for the appearance, spread and number of metastases. However, it was found, especially with ductal carcinomas and adenocarcinomas, that whenever the continuity of the lining cells of the glandular structures was interrupted or (as in ductal carcinomas) the integrity of islands of tumor cells was disturbed and individual, isolated tumor cells began to invade the surrounding mammary tissue, this phenomenon constituted the most definite sign of a high degree of malignant change. Isolated tumor cells exhibiting severe anaplasia, separated from primary basic structures of the individual carcinoma and singly or in small groups invading neighboring regions, must be considered the most important factor. Most of the tumors which produced metastases in the spleen, ovaries and adrenals showed an infiltration of isolated carcinoma cells outside the primary tumor. This was especially true for the mucinous carcinoma of the signet ring cell variety. The occasional small and clinically unnoticed carcinoma may give rise to widespread metastases. There were 4 such cases in their series. Such instances emphasize the importance of carefully palpating the breasts during general examination. There was no apparent difference in the survival of patients given postoperative radiation and of those not receiving such therapy.

Renal Blood Flow and Sympathectomy in Hypertension.—Corcoran and Page record observations on renal blood flow and hemodynamics in 2 patients with essential hypertension treated by Smithwick's method of abdominal sympathectomy. The clinical result of the operation in the first patient seems satisfactory, and, although sufficient time has not elapsed for the second patient to justify a prognosis, it seems likely that the result will be nearly as good. The second patient's maximal blood pressure in the recumbent position is no higher, and in the erect posture it is a great deal lower than it was before the operation. There is no evidence, however, of increased renal blood flow. On the contrary, it has decreased definitely in the first patient and slightly in the second. The decreased renal blood flow in the former is accompanied with an increase of the filtration fraction, probably the result of increased efferent arteriolar constriction. The observations are in accord with experimental data and with those on the effect of renal denervation and sympathectomy in man. It is suggested that the decrease of arterial pressure in man which follows sympathectomy is an expression of denervation of the reactive visceral splanchnic innervation with resultant partial failure of venous return, most evident in the erect position. The decrease of venous return limits cardiac output and thus tends to decrease arterial pressure. The decrease of arterial pressure is in itself an adequate explanation of the clinical improvement which may follow such an operation, since it may prevent further spread of arteriolar lesions. Renal vasoconstriction in cases of hypertension is probably humoral rather than neurogenic in origin. Decreased arterial pressure occurring as a result of sympathectomy may arrest the progress of renal arteriolosclerosis in a hypertensive patient. Since these arteriolar lesions may contribute to the release of renin and the activity of the renal vasopressor system, sympathectomy may interrupt for a time the progress of the disease.

Activity After Operation.—Leithauser and Bergo have performed 383 appendectomies since January 1938. There were 13 cases of ruptured appendix and spreading or generalized peritonitis. The average period of confinement to bed after operation for the other 370 patients was one and a half days and the average hospitalization two and three-tenths days. Fifteen patients had minor wound infections. These patients were not confined to bed for treatment but came to the office for dressings. There were no other complications. During the first twenty-four hours after operation the patients were given 2 ounces (60 cc.) of water every two hours and morphine as required to relieve pain. Enemas and cathartics were not given, but liquid petrolatum was prescribed on the third or fourth day. The patients were turned frequently in bed and were instructed to be active and to take deep breathing exercises at regular intervals. On the first postoperative day they were assisted in sitting on the edge of the bed (after assuming the right lateral position) and then in standing beside the bed for deep breathing exercises. While in each position they were instructed to take several deep inhalations and to cough. They were permitted to walk about the room and to sit in a chair for a few moments and then returned to bed. On returning to bed they sat on the edge of the bed and reclined on the right side. The patients left the hospital by automobile and presented themselves at the office on the sixth postoperative day. Most of the patients selected on the basis of their mental attitude and general well-being were permitted to do light work on the eighth day and to undertake heavy manual labor on the fourteenth. The authors were so impressed by the rapid recovery and freedom from complications of these patients that they have since used the method after other major surgical procedures. The results among 66 patients undergoing cholecystectomy, gastrectomy, gastroenterostomy, pelvic operations, splenectomy, thyroidectomy and other operations were also gratifying. Their average period of confinement to bed was two days and postoperative hospitalization nine days. No dehiscence, hernia, pneumonia, thrombophlebitis or other serious complications (except 1 instance of fatal hemorrhage) occurred. The method decreases atrophy from disuse of the sutured layers and may promote healing by improving the circulation in the area of the wound.

Connecticut State Medical Journal, Hartford

5:403-478 (June) 1941

Weather and the Practice of Medicine. W. F. Petersen, Chicago.—p. 405.
Some Early Medical Teachers in Connecticut. H. B. Ferris, New Haven.—p. 411.
Gastrointestinal Disturbances in Nervous and Mental Disease. B. V. White, Hartford.—p. 425.
Neurologic Lesions That Give Gastric Symptoms. J. C. Fox Jr., New Haven.—p. 429.
Hypernephroma with Metastases to Scapula: Case Report. L. L. Tylec, Waterbury.—p. 432.
Psychiatric Considerations in the Selection of Military Personnel. L. H. Cohen, Norwich.—p. 453.

Illinois Medical Journal, Chicago

79:357-440 (May) 1941

Organization and Function of Tumor Clinics in Voluntary Hospitals. H. P. Saunders, Chicago.—p. 409.
Public Health Aspects of Poliomyelitis in Illinois. J. S. Altman, Springfield.—p. 412.
Paralytic Accidents Due to Rabies Vaccine. L. W. Mason and R. S. Dille, Evanston.—p. 414.
Cholecystitis and Cholelithiasis in Children: Report of Case. R. A. Tearnan, Decatur.—p. 418.
Selection of Cases for Splenectomy. R. L. Haden, Cleveland.—p. 421.
High Spots in Bronchiectasis. P. B. Goodwin, Peoria.—p. 426.
Adequate Control of Menopause. G. L. Perusse Sr. and G. L. Perusse Jr., Chicago.—p. 430.
Sedation and Hypnosis with Minimal Side Reactions. C. J. Molengraft and H. E. Kimble, Chicago.—p. 432.
Adequate Immobilization of Fractures of Leg. W. J. Potts, Oak Park. —p. 434.

Indiana State Medical Assn. Journal, Indianapolis

34:287-354 (June) 1941

Obstetrics—Old and New. H. A. Cowing, Muncie.—p. 287.
Early Physical Therapy in Treatment of Fractures of Surgical Neck of Humerus. G. J. Garceau and Shirley Cogland, Indianapolis. —p. 293.
The Menopause. D. A. Bickel, South Bend.—p. 295.
Endocavitary Aspiration: Monaldi Procedure. F. L. Giles, Kealia, Kauai, Hawaii.—p. 298.
Adequate Laboratory Service to Small Hospitals. B. W. Rhamy, Fort Wayne.—p. 303.
Congo Red—Effective Chemotherapeutic Agent. W. L. Green, Columbus. —p. 306.
Pneumonia. M. E. Thomas, J. Dorman and C. J. Clark, Minneapolis. —p. 308.

Journal of Nutrition, Philadelphia

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Effect of Certain Carcinogens on Vitamin A in Liver. C. A. Baumann, E. G. Foster and P. S. Lavik, Madison, Wis.—p. 431.
Sparing Action of Thiamine on Body Tissue Catabolism. B. Sure and M. Dichek, Fayetteville, Ark.—p. 445.
Riboflavin as Factor in Economy of Food Utilization. B. Sure and M. Dichek, with assistance of M. M. Citron, Fayetteville, Ark.— p. 453.
Vitamin A Deficiency: Field Study in Newfoundland and Labrador. D. Steven and G. Wald, Cambridge, Mass.—p. 461.
Depletion of Tissue Glycogen During Fasting and Fatigue and Partial Recovery Without Food. Pauline E. Nutter, Rochester, N. Y.— p. 477.
Glycogen Formation in Liver and Muscle from Glucose and Fructose After Extreme Muscular Exhaustion. Pauline E. Nutter and J. R. Murlin, Rochester, N. Y.—p. 489.
Studies on Vitamin C Metabolism of Four Preschool Children. Milicent L. Hathaway and Frieda L. Meyer, Ithaca, N. Y.—p. 503.
Biologic Response of Chickens to Certain Organic Acids and Salts, with Particular Reference to Their Effect on Ossification. J. T. Correll, Kalamazoo, Mich.—p. 515.
Study of Vitamin C Nutrition in Group of School Children: Part II. Dietary Evaluation. Elizabeth Murphy, Orono, Maine.—p. 527.

21:541-656 (June) 1941

Effect of Calcium and Phosphorus on Metabolism of Lead. J. B. Shields and H. H. Mitchell, Urbana, Ill.—p. 541.
Respiratory Metabolism in Fructosuria. Henderika J. Rynbergen, W. H. Chambers and N. R. Blatherwick, New York.—p. 553.
*Calcium Requirement of Man: Balance Studies on Seven Adults. Julia Outhouse, Herta Breiter, Esther Rutherford, Julia Dwight, Rosalind Mills and Williamina Armstrong, Urbana, Ill.—p. 565.
*Further Experiments on Calcium Requirement of Adult Man and Utilization of Calcium in Milk. F. R. Steggerda and H. H. Mitchell, Urbana, Ill.—p. 577.
Distribution of Pyridoxine (Vitamin B_6) in Meat and Meat Products. L. M. Henderson, H. A. Waisman and C. A. Elvehjem, Madison, Wis.—p. 589.
Sodium and Potassium Salts in Treatment of Experimental Diabetes and Diabetes Mellitus. S. Strouse, Florence Buel, R. Kay and D. Drury, Los Angeles.—p. 599.
Requirement of Mouse for Pantothenic Acid and for New Factor of Vitamin B Complex. J. G. Sandza and L. R. Cerecedo, New York. —p. 609.
Iron Metabolism in Human Subjects on Daily Intakes of Less Than 5 Mg. Ruth M. Leverton, Lincoln, Neb.—p. 617.
Choline Metabolism: VII. Some Dietary Factors Affecting Incidence and Severity of Hemorrhagic Degeneration in Young Rats. W. H. Griffith and D. J. Mulford, St. Louis.—p. 633.

Calcium Requirements of Adults.—Outhouse and her associates determined the calcium requirement of 7 adults from 21 to 42 years of age. The requirement was computed from data on calcium balances secured at levels of intake almost sufficient to induce calcium equilibrium and from data concerning the extent to which each subject could utilize milk calcium. The requirements, when based on weight, height and surface area, amounted to an average of 10.7 mg. per kilogram. These requirements, calculated on a weight basis of 70 Kg., average 752 mg. This is 67 per cent greater than the 450 mg. requirement suggested by Sherman, whose figure the authors believe is too low because it is predicated on the assumption that adults utilize 100 per cent of their dietary calcium.

Calcium Requirement of Adult Man.—Twenty-five further calcium balance periods from twelve to thirty-two days each were carried out by Steggerda and Mitchell on 9 adult men. The data indicate that Sherman's estimate is too low by reason of the method of derivation, which neglects to consider the close positive correlation between intake and excretion. The common procedure of estimating the prevalence of calcium undernutrition in a population by comparing the estimated calcium content of individual or family dietaries with an average requirement yields extremely dubious data, not only because of individual variability in requirement and utilization of the calcium from different foods, but also because of the great adaptive powers of the human organism. It appears that in the presence of an inadequate supply of any nutrient, including calcium, the body can adjust itself to the situation either by a more economical use of the little available or by a lowering of its own requirements, so that eventually it comes into equilibrium with the limited food supply. Only during this period of adjustment can the body be considered to be undernourished, since only then is it suffering a loss of nutriment. When adaptation is complete, the body replaces from its restricted supply all losses of the nutrient from its body, and, unless some subsidiary ill effects ensue, it may be regarded as adequately nourished.

Journal of Pharmacology & Exper. Therap., Baltimore

72:123-226 (June) 1941

Study of Effects of Morphine and of Carbon Tetrachloride on Rate of Disappearance of Ethyl Isoamyl Barbituric Acid. H. J. Tatum, D. E. Nelson and F. L. Kozelka, Madison, Wis. —p. 123.
Effects of Certain Drugs on Temperature Regulation and Changes in Their Toxicity in Rats Exposed to Cold. J. B. Herrmann, New Haven, Conn.—p. 130.
Excretion of Combined Morphine in Tolerant and Nontolerant Dog. V. Thompson and E. G. Gross, Iowa City.—p. 138.
Toxicity and Local Anesthetic Activity of Three New Biphenyl Derivatives. E. J. Fellows, Philadelphia.—p. 146.
Effect of Atropine, Pilocarpine, Prostigmine, Eserine, Mecholyl and Ephedrine on Tonus and Contraction Mechanisms of Urinary Bladder, with Observations on Clinical Application of These Drugs. H. A. Teitelbaum and O. R. Langworthy, Baltimore,—p. 152.
Influence of Gold Sodium Thiomalate (Myocrysin) on Prevention of Hemolytic Streptococcus Arthritis in Rats. S. Rothbard, D. M. Angevine and R. L. Cecil, New York.—p. 164.
Effect of Barbituric and Thiobarbituric Acid Derivatives on Pyloric Sphincter and Stomach in Unanesthetized Dogs. C. M. Gruber and C. M. Gruber Jr., Philadelphia.—p. 176.
Toxicity of Optically Inactive *d*-and *l*-Selenium-Cyctine. A. L. Moxon, K. P. Du Bois and R. L. Potter, Brookings, S. D.—p. 184.
Toxicity of Orally Ingested Tungsten Compounds in Rat. F. W. Kinard and J. Van De Erve, Charleston, S. C.—p. 196.
Studies on Fat Metabolism and Susceptibility to Carbon Tetrachloride. J. C. Forbes, B. E. Leach and E. L. Outhouse, Richmond, Va.— p. 202.
Quantitative Effect of Fifteen Chemically Related Glycosides and Genins on Embryonic Chick Heart. A. C. DeGraff, New York; G. H. Paff and R. A. Lehman.—p. 211.

Kentucky Medical Journal, Bowling Green

39:197-230 (June) 1941

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Present Status of Immunization in Childhood. J. H. Pritchett, Louisville.—p. 214.
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Maine Medical Association Journal, Portland

32:129-160 (June) 1941

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Medicine, Baltimore

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*Weil's Disease: Complete Review of American Literature and Abstract of World Literature; Seven Case Reports. W. F. Ashe, H. R. Pratt-Thomas and C. W. Kumpe, Cincinnati.—p. 145.
Action of Fluorine in Limiting Dental Caries. J. F. Volker and B. G. Bibby, Rochester, N. Y.—p. 211.
*Favism: Singular Disease Chiefly Affecting Red Blood Cells. A. Luisada, Waltham, Mass.—p. 229.

Weil's Disease.—Ashe and his associates believe that the lower reported incidence of Weil's disease in this country is not due entirely to its less frequent occurrence but that probably because of its protean nature it is not always diagnosed. Most of the American cases occur during June, July, August and September; this concurs with the maximal European incidence, which is in July, August and September. Only 1 nonicteric case has been reported in this country. In Europe, as the disease became better known, the incidence of nonicteric cases rose rapidly, until now analysis shows that not more than 50 per cent have jaundice. As in typhoid, the procedures necessary to diagnose Weil's disease vary and depend on the duration of symptoms. For therapeutic reasons it is most desirable to demonstrate the organism directly in the blood stream in the first week of the disease, when specific therapy (immune serum) is most valuable. As yet American drug houses have not prepared such serums and cannot be expected to do so until city and state laboratories make available the necessary diagnostic procedures and the true incidence of the disease in the United States becomes known. Until immune serums appear on the American market, supportive therapy and convalescent serum or whole blood transfusions should be used when possible. The National Institute of Health at Washington, D. C., is the only public laboratory equipped to do thorough diagnostic and investigative studies on this disease. Weil's disease is primarily an occupational disease now compensable in New York State. The authors report 7 cases of Weil's disease seen within the last year at the Cincinnati General Hospital. All the patients were jaundiced, 5 recovered and 2 died. The postmortem demonstration of organisms in the 2 patients who died confirmed the diagnosis. In the nonfatal cases the diagnosis was proved by specific agglutinations.

Favism.—Luisada suggests that in the future more cases of favism (only 3 have been reported so far) will be recognized in the United States. A large Mediterranean population lives in certain parts of the United States. Fava beans are cultivated extensively in some states (mainly New York, New Jersey, Illinois and California). They are a staple article of diet, being even imported as canned food from Italy. The environment, inhalation, is definitely related to the chief clinical syndromes of favism. Fields of fava beans constitute the usual surroundings in which attacks occur. The pollen is sticky and has no wide dissemination. Attacks caused by ingestion may occur anywhere, but they are more frequent where the custom to consume this vegetable is not occasional. The plant Vicia faba (called in Italian and Portuguese "fava," known in English as the "horse bean," "broad bean" or "fava bean") is the cause of the attacks. The first symptoms after inhalation of principles originated in the flowers or plant of the fava bean usually occur from a few minutes to some hours. After ingestion of fava beans the time element is from five to twenty-four hours. In the sudden attacks caused by inhalation the first symptom is dizziness, sometimes reaching the stage of a collapse. More usually malaise, headache, dizziness and nausea appear gradually. Then repeated yawning, vomiting, chill, pallor and pain in the lumbar region are followed by high fever. The more specific symptoms, hemoglobinuria in from five to thirty hours and icterus in a few hours, appear later. Typical attacks last for from two to six days. Death occurs almost only in children and this during the first two days, seldom on the third day. According to Fermi, the mortality for children is 8 per cent. Of the three theories (parasitic, toxic and allergic) advanced for favism the allergic theory is the most commonly advocated and most logical. Lusena confirmed the allergic mechanisms by pointing out the short duration of the incubation period, the innocuousness of the substance for most individuals and the extremely small doses which may provoke an attack. The allergic theory has since been suggested by many other investigators. Sensitization can occur in persons of any age. Desensitization occurs usually for a short time during and after attacks. Further studies are necessary for the complete explanation of hemoglobinuria. Treatment of the hemolytic attack is important, since it often endangers life and always causes severe anemia. Some of the therapeutic agents used with good results have been normal horse serum, horse serum and mother's blood, mother's blood and intramuscular or intravenous injection of magnesium thiosulfate, epinephrine intramuscularly and calcium gluconate intravenously. Iron may be given, but liver therapy is not indicated. In the absence of specific treatment the most effective preventive measure is the avoidance of contact with fava proteins, especially from April to August.

Michigan State Medical Society Journal, Muskegon

40:241-320 (April) 1941

Dermatitis and Eczema: Industrial Aspects. J. G. Downing, Boston.—p. 265.
Forensic Psychiatry in Michigan. R. M. Patterson, Ann Arbor.—p. 271.
Chronic Nontuberculous Lesions of Lungs. J. E. Lofstrom and F. C. Jewell, Detroit.—p. 272.
Intestinal Suction Drainage in Facilitating One Stage Resection of Right Colon. J. B. Hartzell, Detroit.—p. 277.
Type III Pneumococcus Meningitis: Recovery Following Sulfathiazole. G. B. Myers, J. M. Robb and M. Clapper, Detroit.—p. 280.
Radiation Therapy in Treatment of Malignant Disease of Genitourinary Tract. H. G. Sichler, Lansing.—p. 284.
Acute Gangrenous Cholecystitis in Children: Report of Case in Child Aged 4. L. B. Ashley and A. S. Narotzky, Detroit.—p. 287.
Amebiasis with Pleuropulmonary Complications: Report of Two Cases. G. A. Sherman and H. Weinberger, Pontiac.—p. 289.
Vitamin and Mineral Requirements in Pregnancy. J. H. Musser and W. A. Sodeman, New Orleans.—p. 292.
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40:321-408 (May) 1941

Changing Pictures of Diabetes. R. Fitz, Boston.—p. 345.
Urethral Diverticula and Culdesacs. N. E. Aronstam, Detroit.—p. 355.
Factors in Maternal Health: Hospitals and Staff Groups. S. A. Cosgrove, Jersey City, N. J.—p. 357.
Indications for Simple and Radical Mastoid Operations. H. Brunner, Chicago.—p. 363.
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Military Surgeon, Washington, D. C.

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Medical and Sanitary Care of Civilian Population Necessitated by Attacks from Hostile Aircraft. H. C. Lueth.—p. 597.
Relief of Pruritus by Benzoyl Persulfide, Especially in Dermatitis from Poison Ivy and Insect Bites. S. Amberg and L. A. Brunsting.—p. 617.
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Neuropsychiatric Examination for Induction or Enlistment in the Army. T. J. C. von Storch and G. O. Pratt.—p. 627.
Problems of Ventilation for Vessels of the Navy. A. R. Behnke Jr.—p. 633.
Treatment of Rattlesnake Bite. F. Speer.—p. 640.
Study of Syphilis as Etiologic Factor in Arteriosclerosis and Arterial Hypertension. H. C. Harris.—p. 642.
Treatment of Gonorrhea with Sulfathiazole. H. M. Boslow.—p. 659.
Aid in Differential Diagnosis of Pulmonary Neoplasm. J. L. Dixon.—p. 661.
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Nebraska State Medical Journal, Lincoln

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Cardiac Hypertrophy. J. P. Tollman, Omaha.—p. 215.
Clinical Toxicity of Sulfanilamide and Its Related Drugs. R. J. Wyrens, Omaha.—p. 220.

New Orleans Medical and Surgical Journal

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Recent Advances in Vitamins: Chemistry of Vitamins. A. O. Kastler, New Orleans.—p. 606.
Medical Aspects of Vitamin Therapy. S. B. Nadler, New Orleans.—p. 611.
Significance of Vitamins in Surgery. M. DeBakey and M. C. Smith, New Orleans.—p. 617.
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Northwest Medicine, Seattle

40:109-158 (April) 1941

Factors Responsible for Present Day Low Mortality in Acute Ileus. A. O. Whipple, New York.—p. 112.
Resection of Carcinoma of Rectosigmoid with End to End Anastomosis of Sigmoid to Rectum. O. F. Lamson, Seattle.—p. 117.
Surgical Significance of Fecal Impaction. R. E. Mullarkey, Seattle.—p. 118.
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Rehabilitation After Radical Local Resection of Bone Tumors. J. I. Tuell, Seattle.—p. 138.
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Carcinoma of Cervical Stump. R. E. Watkins, Portland, Ore.—p. 172.
Management of Anorectal Pathology in Obstetrics. J. W. Mounsey, Spokane, Wash.—p. 176.
Gallstone Obstructing Duodenum. M. F. Fuller, Aberdeen, Wash.—p. 180.

40:193-226 (June) 1941

*Traumatic Complete Heart Block of Eighteen Years' Duration, with Review of Literature. T. H. Coffen, H. P. Rush and R. F. Miller, Portland, Ore.—p. 195.
Thromboangiitis Obliterans and Acrosclerosis: Case Report. T. J. Fatherree and C. Hurst, Soap Lake, Wash.—p. 200.
Treatment of Gonorrhea in Male with Sulfathiazole. J. G. Strohm, W. E. Nielsen and P. B. Potampa, Portland, Ore.—p. 202.
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Review of Pneumococcic Meningitis. H. D. Pass, Seattle.—p. 210.
Vitamin B_1 in Chronic Bronchitis. O. J. Morehead, Ritzville, Wash.—p. 212.
The Allergic Nose. N. W. Clein, Seattle.—p. 213.
Metastasis of Carcinoma of Kidney to Heart and Thyroid: Report of Case. W. B. Dublin, Fort Steilacoom, Wash.—p. 215.

Traumatic Heart Block.—Coffen and his associates report the case of a boy who at 3 years of age (in 1922) sustained a severe fall and from then on his mother noticed that his pulse was slow. At examination in 1929 the boy presented a complete auriculoventricular block. He has been seen frequently since 1929 and, while the heart block persists, the boy, now 21, has developed normally, is physically active and has no symptoms of cardiac strain or Stokes-Adams syndrome. In the last ten years he has been examined at least once a year. There have been no changes in the electrocardiogram during this time. The case is unique because (1) it is the only case the authors are able to find in which auriculoventricular block occurred from injury in childhood, (2) there are only 5 other cases in which auriculoventricular block resulted from nonpenetrating injury, (3) it has persisted for eighteen years in their patient and (4) there has been no evidence of heart failure or Stokes-Adams syndrome.

Oklahoma State Medical Assn. Jour., Oklahoma City

34:139-188 (April) 1941

Intracavitary X Radiation. L. S. McAlister, Muskogee.—p. 139.
Chronic Otitis Media. R. W. Rucker, Bartlesville.—p. 144.
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Phorias: Diagnosis and Treatment. J. P. Luton, Oklahoma City.—p. 150.
Use of Sulfapyridine in Treatment of Pneumonia in Children. E. M. Gullatt, Ada.—p. 153.
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34:189-234 (May) 1941

Some Mechanical Factors Involved in Production of Hiatus Hernia of Stomach. E. G. Hyatt, Tulsa.—p. 194.
Reducing Mortality of Cancer. J. B. Hix, Altus.—p. 199.
Acute Retrobulbar Neuritis. D. L. Edwards, Tulsa.—p. 201.
Varicose Veins of Lower Extremities. J. P. Wolff, Oklahoma City.—p. 204.
Clinical Significance of Delayed Osseous Development. B. H. Nicholson, Oklahoma City.—p. 206.

Southern Medical Journal, Birmingham, Ala.

34:559-680 (June) 1941. **Partial Index**

*Familial Darier's Disease (Keratosis Follicularis). J. M. Hitch, Raleigh, N. C.; J. L. Callaway, Durham, N. C., and V. Moseley, Orangeburg, S. C.—p. 578.
Value of Weltmann Serum Coagulation Reaction in Allergic Disease. Susan Coons Dees, Durham, N. C.—p. 586.
Chronic or Healed Pyelonephritis in Negro Women Dying with Hypertensive Heart Disease: Comparative Incidence of This Lesion in Histologic Sections. Thelma B. Dunn, Washington, D. C.—p. 593.
*Acute Osteomyelitis with Staphylococcus Septicemia: Clinical Report on Use of Chemotherapy and Staphylococcus Antitoxin in Its Treatment. L. D. Baker, Durham, N. C.—p. 619.
Observations on Etiologic Relationship of Gastric Juice (Intrinsic Factor) and Foods (Extrinsic Factor) to Blood Pressure. H. M. Doles, Norfolk, Va.—p. 627.
Analysis of Some Cases of Gastrointestinal Allergy Associated with Organic Disease. Gertrude Holmes, Greenville, S. C.—p. 634.
Treatment of Peptic Ulcer with a Magma of Magnesium Trisilicate: Preliminary Report. D. N. Silverman and R. A. Katz, New Orleans.—p. 638.
*Abdominal Arterial Apoplexy. G. H. Bunch and L. E. Madden, Columbia, S. C.—p. 643.
Recurrent Gastrointestinal Disturbances of Early Infancy. W. A. McGee, Richmond, Va.—p. 648.
Encephalitis, Encephalomyelitis and Myelitis: Review of Cases. N. Gotten and G. J. Levy, Memphis, Tenn.—p. 655.
Significance of Collapse Therapy in the Mississippi State Program for the Control of Tuberculosis. J. S. Harter, Sanatorium, Miss.—p. 665.
Modern Standards and Trends in Medical Education. R. U. Patterson, Oklahoma City.—p. 668.

Familial Darier's Disease.—Hitch and his collaborators report the occurrence of Darier's disease in 14 members of one family. Only 6 of the affected members are still alive. The authors were told that the disease in the deceased relatives was identical in regard both to history and to appearance. The family is intelligent and observant and has lived within a restricted region for several generations, so that the information is considered reliable. This family has yielded the largest number of cases of the disease on record. Complete data have been obtained on six generations. There are in all 52 blood kin on whom the authors have sufficient data to be reasonably sure of the presence or absence of this affliction. Of 27 males 4, and of 25 females 10 showed the disease. The average age of the affected dead individuals was 59 as against 47 years for those free of the condition. An examination of the family chart and of those previously reported will show that in familial cases the aberration is transmitted through and to both sexes. The successive appearance of the disease in each generation and its absence in the offspring of normal members rule out the possibility that a simple recessive characteristic is being dealt with. All evidence to date indicates that in the familial cases the abnormality is caused by a single dominant non-sex linked gene. For the isolated case of Darier's disease they believe that the genetic theory which probably best explains this situation is that of "irregular dominance." According to this concept the expression of a certain gene may be modified by another gene or group of genes. The modifiers may enhance or suppress the expression of the character. A gene which is usually dominant may be present in an individual and yet not be phenotypically visible because it has been suppressed by a modifier. It is most probable that one of these situations exists in Darier's disease. In the sporadic patient it must be assumed that the combination is present in toto but is not accessible to examination in other members of his family. The treatment of this condition is uniformly unsatisfactory. Since approximately 50 per cent of the offspring of diseased members will be affected and transmit the disease in similar ratio, avoidance of children by the intelligent patient and sterilization of the unintelligent or uncooperative patient appear justified.

Osteomyelitis and Staphylococcic Septicemia.—Results obtained at Duke Hospital in the treatment of acute osteomyelitis with staphylococcic septicemia suggest that with the exception of sulfathiazole the sulfonamides are contraindicated. The local use of sulfathiazole appears to be beneficial. There were 143 instances of staphylococcemia (86 with osteomyelitis) among 827 proved cases of staphylococcic disease. The present study is concerned primarily with osteomyelitis. Of the 143 instances of staphylococcic septicemia 79 patients died, giving a total mortality rate of 54.5 per cent. Of the 67 patients not treated with staphylococcus antitoxin 51 died and 16 survived, a mortality

rate of 76 per cent; whereas of the 50 patients treated with staphylococcus antitoxin without chemotherapy 16 died and 34 survived, a mortality rate of 32 per cent. Chemotherapy other than sulfathiazole was combined with the antitoxin in the treatment of 16 patients; 5 survived and 11 died. Sulfathiazole was combined with antitoxin in the treatment of 10 patients; 9 survived and 1 died. Of the 86 patients with proved staphylococcic septicemia with osteomyelitis 33 did not receive staphylococcus antitoxin; 11 of these survived and 22 died, a mortality rate of 66.6 per cent; 1 of the 11 who survived received sulfathiazole. Thirty-five patients were treated with antitoxin without chemotherapy; of these 27 survived and 8 died, a mortality rate of 22.5 per cent. There were 9 patients with osteomyelitis and staphylococcic septicemia who were treated with antitoxin and sulfathiazole; 8 survived and 1 died. Of 9 patients treated with antitoxin and chemotherapy other than sulfathiazole, 6 died and 3 survived. In hemolytic staphylococcus infections the ratio of mature to immature polymorphonuclear leukocytes in the circulating blood can be used to estimate the degree of toxemia and to determine the need for antitoxin. Highly purified antitoxin serum can be administered intravenously if the necessary precautions to determine the patient's sensitivity have been taken. Sulfanilamide and sulfapyridine are contraindicated.

Abdominal Arterial Apoplexy.—Bunch and Madden report the seventeenth case of abdominal apoplexy. The diagnosis was made from the history of marked arteriosclerosis in an elderly (62 years of age) Negro having abdominal crises with shock, followed by abdominal swelling, and from the finding of intraperitoneal blood by paracentesis, with a hemoglobin content higher than that of the capillary blood. Treatment immediately following the abdominal attack is that of internal hemorrhage. After reaction from shock has taken place, enough blood should be given by repeated transfusions to raise the blood pressure and the hemoglobin index to within operable limits. At laparotomy, if the patient is a woman of childbearing age, the pelvis should be examined for tubal abortion or rupture. In men without aneurysm or malignant neoplasms, spontaneous rupture of the spleen, the liver or the pancreas is the most common cause of nontraumatic intra-abdominal bleeding. In spontaneous arterial rupture the bleeding point should be found and hemorrhage controlled by ligature or suture, and if neither is possible by gauze pack. Every 1 of the 16 cases of spontaneous rupture of a visceral artery with massive hemoperitoneum reported in the literature has had arteriosclerosis as a base.

Tennessee State Medical Assn. Journal, Nashville

34:161-204 (May) 1941

*Treatment of Penetrating Wounds of Brain. C. Pilcher, Nashville.—p. 166.
Treatment of Bacillary Dysentery with Sulfathiazole: Report of Nineteen Cases. R. E. Ching, O. S. Warr Jr. and J. B. Witherington, Memphis.—p. 171.
The Physicians in the National Defense. A. G. Love, Washington, D. C.—p. 178.
Remarks. F. H. Lahey, Boston.—p. 184.
Pediatric Emergencies. K. M. Buck, Memphis.—p. 186.
Allergy and Its Relation to Sinusitis. C. H. Glover, Memphis.—p. 188.

Treatment of Penetrating Wounds of Brain.—Pilcher points out that most penetrating wounds of the brain in civilian and in military life are cared for by the general surgeon, who should remember that every compound fracture of the skull is potentially a penetrating wound of the brain. Treatment should not be attempted without adequate neurosurgical facilities. First aid should consist of superficial cleansing and shaving, control of hemorrhage and treatment of shock. Most important is rapid transportation to a point at which operation can be performed. During transportation the head should be moderately elevated (unless shock is present). Evacuation of the wounded by airplane, as it is now practiced by the German army, has met with considerable success. However, in open head wounds the low atmospheric pressure of high altitudes may increase cerebral herniation. In the author's experiments, immediate removal of foreign bodies in twelve hours resulted in 75 per cent recovery and their removal after twenty-four hours resulted in 75 per cent fatality. The complete removal of foreign bodies is not always feasible or wise. Great depth of penetration or lodgment in the opposite hemisphere from the point of entrance renders removal difficult, and the damage caused thereby is too great to justify the procedure. The bullet itself is not often a source of pathogenic bacteria. Contamination is much more likely to arise from fragments of skin, hair, clothing, dirt and other material that has been driven in. If cleansing is complete and damaged tissue thoroughly removed, and if the wound is closed within a few hours the danger of a retained projectile is minimized. The brain tolerates foreign bodies well. The author cites 2 cases which support the rational advice of Cushing that foreign bodies should be removed only if their removal does not increase the existing cerebral damage. The location and depth of the wound influence not only the degree of residual disability, if the patient recovers, but his chances of recovery. In addition to the high mortality resulting from laceration of large arteries or the great venous sinuses, penetration of the ventricular system (particularly if early operation is not possible) and injury of the brain stem, midbrain or hypothalmic region are of grave prognostic importance; they usually terminate fatally. These structures may be unexpectedly involved by seeming distant wounds. For patients not seen until frank infection is present (or in the borderline period from twelve to twenty-four hours when infection may develop) immediate open drainage offers the only hope of avoiding a fatal outcome. The bony opening should be from 3 to 4 cm. in diameter, the dura left open and a soft tube or even small gauze packing inserted to the bottom of the cavity. The once dreaded cerebral fungus will develop. However, the danger from it is in reality small if drainage is adequate and the cerebral infection becomes localized. For the patient seen after healing of such an infection because of convulsions, paralyses or other disabling symptoms, excision of the cicatricial mass is indicated. The author states that, for traumatic neurosurgery, carefully trained and experienced operative teams and elaborate equipment, though desirable, are not essential. However, two devices, a strong suction apparatus and a high frequency, damped-wave electrosurgical unit, are almost indispensable. Without them adequate débridement and control of hemorrhage are all but impossible. All macerated scalp tissue, free fragments of bone, devitalized brain tissue and accessible foreign material should be removed, but the injury already sustained should not be increased. Gentle irrigation will "float up" all but the largest foreign fragments, and careful suction will cleanse the tract and facilitate complete hemostasis. Temporary gentle packing with moist cotton may be useful. Gauze should never be used on the brain. All wounds free of infection should be closed tightly with fine silk. A drain inserted into the brain is an open invitation to infecting organisms, and it increases the danger of cerebral herniation. If loss of skin has been extensive, it may be possible to close the defect by "relaxation incisions." The exact field of usefulness and the true effectiveness of the sulfonamide drugs in craniocerebral wounds contaminated by bacteria have not yet been finally determined. The Canadian and German armies are using them for prophylaxis and therapy. Extensive studies on the subject are in progress.

Virginia Medical Monthly, Richmond

68:313-374 (June) 1941

Pollen Survey of Islands of Bermuda. L. N. Gay, H. Curtis and T. Norris, Baltimore.—p. 313.
Mediastinal Emphysema and Idiopathic Spontaneous Pneumothorax. M. M. Pinckney, Richmond.—p. 315.
Unusual Tumors of Brain, with Emphasis on Pathologic and Diagnostic Pitfalls: Report of Five Cases. J. M. Meredith, University.—p. 319.
Diagnosis and Selection of Treatment for Carcinoma of Larynx. E. T. Gatewood, Richmond.—p. 330.
Intestinal Implantation with Lactobacillus Acidophilus by Use of Bacillus Acidophilus Milk. J. D. Willis, Roanoke.—p. 336.
Abnormal Sexual Reactions. J. N. Williams, Richmond.—p. 338.
Quinine as Prophylactic Against Influenza: Study of 6,500 Quininized and 6,500 Nonquininized Individuals During Influenza Epidemic of January 1941. A. G. Schnurman, Radford.—p. 341.
Birth Injuries from the Viewpoint of the Obstetrician. W. D. Suggs, Richmond.—p. 342.
Oral Primary Foci of Infection from Dental Viewpoint. F. G. Repass, Roanoke.—p. 347.
Medical Treatment of Nontuberculous Infections of Kidney and Urinary Tract. R. D. Bates Jr., Richmond.—p. 350.
Acute Hemolytic Anemia and Renal Insufficiency of Sulfanilamide and Sulfapyridine Therapy. G. B. Craddock, Lynchburg.—p. 353.
Platyspondyly. H. G. Hadley, Washington, D. C.—p. 357.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Experimental Pathology, London

22:59-110 (April) 1941

Serologic Reactions of Viruses Causing Tobacco Necrosis. F. C. Bawden.—p. 59.
Healing of Experimental Wounds Treated with Epicutan. L. Dann, A. Glücksmann and Katharine Tansley—p. 70.
Fibrotic Nodules in Tracheobronchial Lymph Glands of Mouse Produced by Breathing Precipitated Silica. J. A. Campbell.—p. 76.
Observations on Factors Concerned in Sedimentation of Erythrocytes. T. N. Fraser and J. B. Rennie.—p. 81.
Spread of Infection from Respiratory Tract of Ferret: I. Transmission of Influenza A Virus. C. H. Andrewes and R. E. Glover.—p. 91.
Id.: II. Association of Influenza A Virus and Streptococcus Group C. R. E. Glover.—p. 98.
Tyraminase Activity in Hypertensive Animal. G. M. Brown and B. G. Maegraith.—p. 108.

British Medical Journal, London

1:617-658 (April 26) 1941

*Successful Grafting of Adrenal Gland in Case of Addison's Disease. F. Katz and F. Mainzer.—p.617.
Treatment of 100 War Wounds and Burns. J. A. Ross and K. F. Hulbert.—p. 618.
Simple Method of Estimating Prothrombin Capillary Blood. J. Innes and L. S. P. Davidson.—p. 621.
Mule Spinner's Cancer. E. M. Brockbank.—p. 622.
Derris Root Treatment of Scabies. L. Saunders.—p. 624.
Subcutaneous Ligature of Varicose Veins. H. S. Russell.—p. 626.

Grafting of Adrenal in Addison's Disease.—Katz and Mainzer discovered only 5 instances of successful adrenal grafting in Addison's disease. They add to this list a sixth instance of successful grafting in an indisputable case of Addison's disease. The patient was under their care for nearly three years before operation and for fifteen months after. Just before the operation the amount of extract necessary was 40 cc. daily, but still the blood pressure dropped to 70 mm. In this crisis it was decided to graft into the patient the left adrenal gland of a man who had just died from a cerebral tumor. The donor was 52 years of age and belonged to the same blood group. The graft was made into the abdominal musculature on the left side. Soon after operation symptoms of adrenal insufficiency, such as increased somnolence, uncontrollable vomiting, frequent diarrheal stools, collapse of circulation and fall of blood presure to 60 mm., reached their climax despite daily administration of extract up to 80 cc. and that of salt up to 50 Gm. The condition improved within three days of the operation, the dose of extract was reduced and none was given after the seventh day. The patient declared that she felt well. She left the hospital on the sixth postoperative day. During the next two months the blood pressure varied between 115 and 135 mm., the color of the skin, which was yellowish with a clay tinge, became lighter and the freckle-like spots present on the backs of her hands and face were no longer so intensely colored. Any great exertion or excitement always produced slight somnolence and pain in the back. During an attack of influenza, when the blood pressure dropped to 80 mm., from 10 to 20 cc. of adrenal extract was necessary for a few days.

1:659-698 (May 3) 1941

Injury and Internal Disease. G. F. Walker.—p. 659.
*Reactions After Transfusion of Stored Blood. E. C. O. Jewesbury.—p. 663.
Carriers of Tuberculosis. J. Maxwell.—p. 665.
Pelvic Abscesses: Diagnosis and Treatment. H. Dodd.—p. 667.
Agranulocytosis in Infant: Case; Recovery. H. C. Barlow.—p. 669.

1:699-738 (May 10) 1941

Pulmonary Tuberculosis in Recruits: Further Experience in Survey by Method of Miniature Radiography. D. Galbraith.—p. 699.
Bacteriologic Examinations Supplementing Radiologic Survey of Australian Imperial Force: Preliminary Report. R. Webster.—p. 701.
Blood Platelets and Splenic Extracts. G. M. Watson.—p. 704.
Evaluation of Hysterical Symptoms in Service Patients. W. P. Mallinson.—p. 706.
Stability of Tetanus Antitoxin Under Suboptimal Storage Conditions. C. R. Amies.—p. 709.

Reactions After Transfusion of Stored Blood.—Jewesbury points out two complications which may develop after transfusion of fresh or stored blood as a result of an incomplete understanding of the technic of blood transfusion. They are pulmonary edema with cardiac failure due to overloading of the circulation of a patient whose heart is already embarrassed, and renal failure due to transfusion of incompatible blood. The reaction more usually apt to occur after a transfusion is a febrile one. Transfusion reactions are divided into grade 1, a rise of temperature to 100 F., with no other objective features; grade 2, a similar or greater rise of temperature, with a subjective feeling of cold and shivering, and grade 3, fever with a definite rigor. The average incidence of grade 3 reactions in three careful investigations on the use of fresh blood for 700 patients was 7.9 per cent. After transfusion of stored blood the average incidence of grade 3 reactions among more than 5,000 transfusions was 5.6 per cent. The use of 700 bottles of stored blood (average age of the blood was ten and eight-tenths days) from the North-East London depot gave 11.3 per cent grade 1, 4.4 per cent grade 2 and 4.1 per cent grade 3 reactions. In this series the author observed that the average age of the blood causing grade 2 reactions was thirteen and four-tenths days, while that of the blood causing grade 3 reactions was twelve and seven-tenths days. There were 4 instances of urticaria resulting from transfusion of stored blood. Six cases of jaundice seemed to be the result of transfusion of somewhat older blood, since all but one of the bloods used was stored for fourteen or more days. Since even fresh blood contains many aged erythrocytes, rapid destruction of these is to be expected after their transfusion. The degree of destruction increases with the age of the blood. As a routine blood preserved for more than three weeks should not be used, since both in vitro and in vivo hemolysis may result in transient jaundice and possibly be the cause of other reactions. Bushby, Kekwick, Marriott and Whitby have shown that the increase in plasma bilirubin of the recipient is due not to free hemoglobin in the transfused blood but to in vivo hemolysis of transfused cells. It is likely that the febrile reactions after transfusion of old blood are due to products of disruption and degeneration of erythrocytes rather than to the free hemoglobin present in solution. The preservative solutions should be those most likely to prevent the early breakdown of erythrocytes. Hemolysis is impeded by dextrose. In the transfusion of 50 bottles of blood (33 transfusions) preserved for an average of eleven and one-tenth days without dextrose the results were, respectively, 18.2, 15.1 and 12.1 per cent grade 1, 2 and 3 reactions. There were also 1 instance of urticaria and 1 of jaundice. The ready availability of stored blood outweighs any slightly smaller rise of hemoglobin percentage that may occur in the recipient. The disadvantage of stored blood resolves itself about hemolysis, but with modifications of the preservative solution the life of the erythrocytes can be further prolonged. There is now less need to preserve emergency supplies of blood for long periods, as plasma or serum, which can be stored for months, can be given as an emergency measure when whole stored blood is not available.

Glasgow Medical Journal

17:141-172 (May) 1941

*Glycosuria in Recruits. A. A. F. Peel and Mary W. Peel.—p. 141.

Glycosuria in Recruits.—The Peels state that 115 instances of glycosuria have been referred to them by three medical boards during thirteen months. They encountered cases which cast doubt on the wisdom of placing too much reliance on a sugar tolerance curve in differentiating between diabetic and innocent glycosurias. The fact that emotion influences the suprarenals, the thyroid and other endocrine glands indicates that it is also probably capable of producing temporary alterations in the sugar tolerance curve. Diet affects the curve, a factor difficult to assess in recruits. A full medical history and a clinical examination are imperative, and a specimen of blood should be taken forty-five minutes after the test dose of dextrose as well as the routine specimens; without this specimen, a diagnosis of renal glycosuria is not justified and a diagnosis of "lag curve" may be mistaken. Diabetic curves (more than 180 mg. in all specimens or more than 200 mg. in one) were obtained in 43 of the 115 recruits, borderline diabetic curves in 9 and lag curves in 12, and 59 had low renal thresholds (blood sugar below 180 mg. per hundred cubic centimeters). Two of the 59 had diabetic curves, 4 borderline diabetic curves and 4

MacLean's lag curve, and 3 others were excluded from consideration because of insufficient data. Among the 46 remaining recruits with renal glycosuria the blood sugar curve of 30 was normal and 16 had abnormal features, although the maximal level never exceeded 180 mg. per hundred cubic centimeters. Of the 30 having renal glycosuria with a normal blood sugar curve, 14 were admitted because of symptoms suggesting diabetes; 4 denying thirst, polyuria and loss of weight were admitted because of other suggestive symptoms, and 12 had no symptoms suggestive of diabetes, but 2 had chronic nephritis. One had fever and tachycardia, 1 a gross cranial deformity and 1 a history of attacks of colic; 1 was below average weight but of good "physique," the general condition of 1 was "fair" and the general condition of 5 was good. Of the 16 recruits having renal glycosuria with abnormal blood sugar curves, 4 had symptoms suggesting true diabetes, 4 seemed susceptible to infections and 8 patients had no diabetic symptoms, but 5 of them suffered from some other form of ill health: anemia, hypertension and albuminuria, slight cardiac enlargement of doubtful cause or nervousness and tremulousness. Nineteen of the 43 with diabetic curves admitted diabetic symptoms; 9 denied thirst, polyuria and loss of weight but seemed to have a susceptibility to boils or cutaneous infections, 15 denied all diabetic symptoms, including susceptibility to boils, but 5 complained of neurasthenia, duodenal ulcer, chronic otitis media or acute rheumatism and pleurisy. No compunction was felt in rejecting as unfit for service those patients who admitted diabetic symptoms and those who suffered from some other complaint. Only 2 of the 9 recruits with borderline diabetic curves admitted diabetic symptoms. Of these 9, 4 had low renal thresholds. Nine of the 12 with lag curves admitted diabetic symptoms on cross examination. The prevalence of thirst, polyuria or loss of weight among these 12 exceeded that of patients with a diabetic type of curve.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

48:1-140 (Feb.) 1941

Normal Menopause. H. C. McLaren.—p. 1.
Induced Menopause. H. C. McLaren.—p. 23.
Uroselectan B as Method of Inducing Labor. P. L. Playfair.—p. 41.
Plasma Uric Acid and Urea Findings in Eclampsia. M. D. Crawford. —p. 60.
Chronic Cornual Disease: Its Symptomatology and Pathology. J. R. Goodall and J. E. Ayre.—p. 73.
Surgical Procedures in Relation to Inflammatory Cervical Pathology. J. R. Goodall and F. O. Anderson.—p. 78.
Sacral Anesthesia in Obstetrics. W. H. Poole.—p. 84.

48:141-292 (April) 1941

Histidine Metabolism in Normal and Toxemic Pregnancy: Excretion of Histidine in Normal Pregnancy Urine and in Urine of Patients with Toxemia of Pregnancy. R. Kapeller-Adler.—p. 141.
Significance of Isolation of Histamine from Urine in Toxemia of Pregnancy. R. Kapeller-Adler.—p. 155.
Evaluation of Treatment of Albuminuria of Pregnancy by Water Balance Method, Assuming the Theory of Water Intoxication in Pregnancy. J. S. G. Wilson.—p. 161.
Ocular Complications in Hyperemesis Gravidarum. A. J. Ballantyne. —p. 206.
Gynecologic and Puerperal Thrombophlebitis Contrasted with Phlegmasia Alba Dolens. J. R. Goodall.—p. 220.
Puerperal Retention of Urine Causing Traumatic Rupture of Bladder and Death: Case. A. M. Claye, with pathologic notes by N. Lissimore.—p. 235.
Carcinoma of Cervix in Girl 15 Years of Age. W. F. Shaw.—p. 239.
Carcinoma of Body of Uterus: Unusual Case. A. M. Claye.—p. 243.
Ectopic Liver Tissue in Newly Born: Case. D. A. Sanford.—p. 246.
Late Postpartum Eclampsia: Case. Eileen M. Whapham and J. S. Hogg.—p. 249.
Diagnosis of Dicephalic Monster by Antenatal X-Ray Examination. Elizabeth F. Hunter.—p. 251.

Lancet, London

1:623-654 (May 17) 1941

Absorption of Bacteria, Toxins and Snake Venoms from Tissues: Importance of Lymphatic Circulation. J. M. Barnes and J. Trueta. —p. 623.
Tuberculous Obstructive Emphysema in Children. B. Barsby.—p. 627.
Recovery from Infection of Subacute Bacterial Endocarditis Without Sulfonamides. F. P. Weber.—p. 630.
Epileptics in Air Raids. J. T. Fox.—p. 631.
Effects of Air Raids on Incidence of Fits in Epileptics. J. Shafar.—p. 632.

Medical Journal of Australia, Sydney

1:537-564 (May 3) 1941

Modern Aspects of Puerperal Sepsis. A. M. Hill.—p. 537.
Report on Cerebrospinal Meningitis. M. J. Holmes.—p. 541.
*Meningococcic Infection, with Special Reference to Meningococcic Septicemia. G. C. Moss.—p. 548.

1:565-596 (May 10) 1941

Minor Surgical Affections of Anal Canal. H. C. R. Darling.—p. 565.
Changes in Muscle Produced by Nerve Degeneration. J. C. Eccles. —p. 573.
Normal Apical Precordial Lead of Electrocardiogram. K. Maddox. —p. 575.
Right Sided Visceroptosis. A. E. Lee and L. J. J. Nye.—p. 578.

1:597-628 (May 17) 1941

Toxemic Pregnancy in Relation to Subsequent Pregnancies, with Special Reference to Renal Function Tests. Vera I. Krieger and R. M. Rome.—p. 597.
Note on Influence of Surgical Operations on Diphtheria Antitoxin Content of Blood Serum. E. Singer.—p. 613.

Meningococcic Infection.—Moss states that failure to obtain organisms in blood cultures is of no significance when typical signs and symptoms of meningococcic septicemia are present. Treatment should not be withheld too long. More widespread knowledge of the significance of the typical rash in conjunction with other symptoms will lead to a diagnosis in many cases at the first examination. This is of great importance today, as sulfapyridine is capable of bringing about a speedy cure. This prompt therapeutic response is an additional diagnostic feature. Results with sulfapyridine in meningococcic meningitis have been spectacular, and it was to be expected that they would be even better in the slow forms of septicemia without meningeal localization. A disease that may entail weeks or months of illness and may end in meningitis or even meningococcic endocarditis with or without other complications can scarcely be called benign in spite of a strong tendency to spontaneous cure. For immunologic reasons more cases are likely to be encountered in the later stages of an epidemic. His first case was one of chronic meningococcic septicemia, lasting at least thirty-three days and terminating in meningitis. Progress was uninterrupted except for nausea from the sulfapyridine. The patient was allowed up on the fourteenth day and, at the time of writing, is quite well. The second patient was treated with sulfapyridine for six days, receiving a total of 23 Gm. of the drug. Thirteen days after chemotherapy was instituted examination of a nasopharyngeal swab did not reveal Neisseria meningitidis. The onset of subacute and chronic forms of meningococcemia is usually, but not invariably, sudden, with malaise, shivering, pains in the limbs, especially the legs, and recurrent headache of varying intensity. This is true also of meningeal signs. Pain in the extremities is not necessarily confined to joints; a joint effusion may or may not be present. With the shivering and rise of temperature there may be a profuse cutaneous reaction and attendant discomfort, yet the patient may feel quite well with the fall of temperature. This comparative well-being has impressed most of those who have seen such patients. The temperature may resemble that of malaria or it may be of the common "septic" type. The rash of meningococcemia, once seen, is not likely to be forgotten. Minor variations exist, but in general the same basic pattern is present. The lesions consist of pink or red macules and papules from a pin's head to a threepenny piece in size; a few larger lesions are often present. The smaller ones are roughly circular; the larger ones are often longer than they are broad. The large ones are usually tender. The limbs are usually most affected; but lesions are commonly seen on the back and chest, sometimes the abdomen and more rarely the face. The color may be uniform or the center more vivid. Complete disappearance with pressure is the rule, except when there is a petechia in the center. Isolated petechiae may coexist. Tender papules or nodes may be found on the shins. They may be confused with erythema nodosum or erythema multiforme. The lesions usually fade in a day or so, some completely, or a faint brown stain of some may persist for some days. At intervals, often corresponding with fever, other lesions may appear. Herpes labialis carries as much diagnostic weight as it does in meningitis.

Schweizerische medizinische Wochenschrift, Basel

71:169-192 (Feb. 22) 1941

Oxygen Capacity of Hemoglobin in Conserved Blood. H. Fischer and O. Schürch.—p. 169.

Utilizability of Conserved Blood as Determined in Point of Time by Loss of Potassium from Erythrocytes. H. Fischer.—p. 173.

*Oral Chemotherapy in Gonorrhea Based on Personal Experiences. G. Miescher and A. Schnetz.—p. 175.

Age Determination of Spinal Fractures. W. Jaeger.—p. 179.

Inoperable Carcinoma and Its Treatment. A. I. Jarotzky.—p. 181.

Sulfathiazole for Gonorrhea.—Miescher and Schnetz present conclusions regarding the effect of single and fractionated doses of sulfathiazole in the treatment of gonorrhea. They found that while single massive doses (3 Gm.) yielded cures amounting to 89.5 per cent (thirty-four cures in 38 cases), fractionated doses, distributed over one, two or six days, gave still better results, namely 97.5 per cent (forty-one cures in 42 cases, in which 1 Gm. was administered seven times for one day at intervals of two hours); 98 per cent (fifty-five cures in 56 cases, in which 1 Gm. was administered five times daily for two days), and 97.5 per cent (eighty-one cures in 83 cases, in which 1 Gm. was administered seven, six and five times daily during six days). Experiments undertaken in 35 cases by increasing the single massive dose from 3 Gm. to 5 Gm. not only failed to produce better results but seemed to suggest chemotherapeutic "fastness," though blood and urine analyses did not indicate a decrease of absorption or an increase of excretion. In additional appraisals of the therapeutic value of single and fractionated doses involving uncomplicated gonorrhea, the authors found that a minimal daily dose of 0.5 Gm. given daily for four days achieved the same results as the same total doses (2 Gm.) given at one time (seven cures in 9 cases). No close connection was observed to exist between drug concentration levels in the blood and recovery. However, higher concentration levels more frequently, on the average, accompanied the cure. Laboratory tests for bacterial chemoresistance in cases which did not respond to treatment demonstrated a temporary bacteriostatic effect of the drug in the face of bacterial multiplication observable in the pus. Chemosensitivity was seen to be extremely variable in different strains, fluctuating strongly within concentration limits of 1:1,000,000 and 1:600. The most chemoresistant strain was derived from a patient who recovered. Cultures on ascitic agar likewise showed considerable variation with regard to the antibacterial potency of different serums. Some gonococci were almost serum fast, others showed extraordinary serum sensitivity. According to the authors, the therapeutic effect of sulfathiazole must be sought not only in the combined interplay of high drug concentration levels, bacterial chemosensitivity and the antibacterial properties of the serum but also in other factors, among which the individual degree of immunity seems to be the most important. Massive single doses may constitute the dosage of choice for patients who cannot be relied on to carry out instructions.

71:213-236 (March 8) 1941. **Partial Index**

*Local Application of Sulfathiazole in Treatment of Accidental Trauma. W. Brunner and E. Schläpfer.—p. 213.

*Experiences with Sulfathiazole in Obstetrics and Gynecology. H. Winzeler.—p. 217.

*Local Sulfathiazole Therapy in Gynecology. J. Flagg and P. Koenig. —p. 220.

Local Sulfonamide Therapy and Sulfathiazole Inunction. A. Schnieper. —p. 222.

Local Sulfathiazole Therapy in Wounds.—Brunner and Schläpfer discuss the therapeutic value of locally applied sulfathiazole as observed in 109 cases of trauma with varying degrees of tissue damage, the majority of which were head wounds (51) and face and limb cuts (18). The drug was used in powdered form (20 cases) and in combination with boric acid (89 cases) in a 20 per cent concentration. This was insufflated on and into the wound. The quantity of the drug used ranged between less than 1 and 7 Gm., according to the nature of the lesion. Wound excision was not practiced; ragged edges were merely trimmed. Immobilization and serum prophylaxis were regularly employed. No inflammatory reactions, no cellular or tissue damage and no delay in recovery were noted. No difference in results was seen when sulfathiazole was used alone or with boric acid. Microscopic tissue examination after administration disclosed distinct bacteriostatic and bactericidal effects. The growth of hemolytic streptococci, Bacillus mesentericus and Bacillus subtilis was controlled by the drug. Hemolytic staphylococcus aureus, nonhemolytic streptococci, Bacterium coli and enterostreptococci were reduced respectively in virulence to 21, 36, 16.6 and 33 per cent and Fränkel-Welchii bacillus to 13 per cent. The therapeutic value of sulfathiazole used locally lies in the antibacterial effect produced by the combination of high concentrations with slow solubility, which is suited to the latent period preceding bacterial invasion of the tissue. Hence the sooner the drug is applied to the wound the better. The authors regard a 20 per cent strength as too powerful for puncture wounds with narrow openings and recommend injections in aqueous solution or a 2 to 5 per cent administration of sodium sulfathiazole. In multiple lesions 0.5 Gm. per kilogram of body weight is well tolerated locally and systemically.

Sulfathiazole Therapy in Obstetrics and Gynecology.—Winzeler's report covers 200 cases observed during a period of eight months. In order to determine the prophylactic value of sulfathiazole in normal births, the author treated a number of pregnant women and controls with a total dosage of 10 Gm. during five days. In another series of 120 pregnancies (half acting as controls) he increased the total dosage to 11.1 Gm. In both series, judged by fever indications and the number of days intervening between rising after delivery and discharge from the hospital, with urinalyses made after delivery and a week later, no difference in results could be determined. In 40 puerperal cases with labor complications (forceps delivery [15], intrauterine intervention [14], cesarean section [11]) concentrated doses ranging between 17 and 26 Gm. and given in accordance with the same criteria, the action of sulfathiazole was regarded as favorable. In a gynecologic group of about 20, the rarity of septic abortion and the absence of bacillary indications in the blood did not furnish enough data for therapeutic appraisal. Sulfathiazole administered *sub partu* was found in the blood and amniotic fluid of the child, but no regular connection between the sulfathiazole levels of the child and the mother could be established. There was little secretion of the drug in the mother's milk. Numerous blood and urine tests showed no hemopoietic or renal damage. No serious sequels resulted from doses as high as 60 Gm. The author does not consider the use of sulfathiazole indicated in normal delivery. The drug seems to possess considerable therapeutic value in cases of light and mildly severe puerperal infection. Its efficacy in grave cases is limited, since secondary foci have already established themselves. The drug should not be given until signs of infection appear. Sulfathiazole was found to be readily tolerated, of moderate toxicity and well adapted for prolonged use, as in cystitis.

Local Sulfathiazole Therapy in Gynecologic Cases.—Flagg and Koenig report 14 cases of cervicitis, 9 of which were associated with adnexitis, in which sulfathiazole could be applied locally with sufficient regularity to bring about 9 cures and 5 improvements in leukorrheal and other vaginal discharges, together with relief from pain. Nine additional cases were favorably affected in spite of irregular or incomplete medication. The dosage was put up in special form and inserted into the cervical canal adjacent to the infected glands in quantities and at intervals adjusted to the individual case. Cervicitis was due thrice to childbirth, twice to abortion and four times to gonorrhea; in the other cases the etiologic factor was unknown. Cures were effected even in chronic cases (four years, twelve years). The authors were induced to experiment with local medication by the fact that oral use had often yielded only slight and temporary relief in spite of heavy dosage. They found that the local application not only spared the general system the pharmaceutic effects but achieved results in much smaller quantities in cases in which much

larger locally administered quantities had failed. A case is cited in which 0.6 Gm. given locally cured where a total of 40 Gm. given orally had proved unavailing. In 8 of the 9 cases of adnexitis, the disappearance of leukorrhea was accompanied with adnexal amelioration, obviously because the drug exerted its potency on the adnexa by way of utero-ovarian lymphatics. Complications were few. First applications, however, seemed to cause a temporary mechanical irritation quite apart from their antibacterial action.

Policlinico, Rome

47:341-384 (Sept.) 1940. Med. Sec. **Partial Index**

*Lymphatic Tissues of Rhinopharynx in Hypertrophy of Thymus After Roentgen Irradiation of Thymus. S. Lentini and A. Cirenei.—p. 359.

Hypertrophy of Thymus.—Lentini and Cirenei observed 19 prepuberal children with hypertrophy of the thymus and the thymic syndrome of obesity, genital hypoplasia, retarded puberty and intelligence, and hypertrophy of the lymphatic and adenoid tissue of the nasopharynx. Pharyngoscopic examination and biopsy of the palatine tonsil were made before roentgen irradiations of the thymus, repeated four or five months after the last irradiation. The patients did not have opotherapy or other treatment in the course of the observation. Irradiations were given every other day in doses of from 90 to 100 roentgens for each irradiation, up to a total of four irradiations, this being followed by twenty days of rest and a new course until three had been given. Irradiations were given at a distance of 30 cm. with rays obtained with 150 to 180 kilowatts and 4 milliamperes, through a filter of 0.5 mm. of copper and 0.3 mm. of aluminum. Care was taken to shield the tonsillar region from the irradiating cone. Except for 1 syphilitic child, treatment resulted in marked improvement of the general, physical and mental condition of the patients as manifested by loss of fat, increase in stature, growth of genitalia, initiation of puberty, normal behavior and intelligence. The nasopharyngeal lymphatic tissues regressed proportionally to the general improvement. The authors reported in a previous article that the removal of the thymus in dogs caused regression of nasopharngeal lymphatic tissues. Clinical observations agree with the animal experiments. The authors point out the advantages of roentgen irradiation of the hypertrophied thymus. The syndrome caused by thymic hypertrophy as well as the hypertrophy of the nasopharyngeal lymphatic and adenoid tissue are controlled by irradiation.

48:337-384 (Feb. 24) 1941. Pract. Sec. **Partial Index**

*Roentgen Irradiations of Thymus in Pende's Hyperthymic Syndrome: Technic and Results. G. A. Calabrese.—p. 337.

Roentgen Treatment of Hyperthymism.—Calabrese describes the mental, genital and somatic syndrome caused by hyperfunetion of the thymus occurring in childhood. It becomes more evident at puberty. The syndrome consists of arrest of the psychic and somatic development of the person, psychic and somatic infantilism, obesity, retardation of puberty, reversal of sexual characteristics and similar changes. There is a hyperplasia of the lymphatic tissue, especially of the thymus, hypoplasia of the genital organs and cryptorchism. The thymus is enlarged, but the enlargement cannot be recognized roentgenoscopically or by insufflation of air or oxygen into the anterior mediastinum. The diagnosis is made from clinical symptoms and signs of enlargement of the thymus obtained on percussion of the thymus area. The treatment consists of roentgen irradiation of the region of the thymus, given in four series twenty days apart. Each series consists of four exposures of 80 or 100 roentgens given every other day. The author administered this treatment to 377 patients (335 boys and 42 girls) of ages from 4 to 12. Endocrine and physical therapy had failed previously. The roentgen treatment alone, or with temporary administration of glandular preparations, brought about improvement in the general condition of all patients and a complete cure in 90 per cent. By cure the author means disappearance of the abnormal and reestablishment of the normal general, genital, somatic, sexual and mental states. Menstruation appeared in girls of puberal age or before they reached the age of 20 within two months after treatment was begun, and after two months in girls over 20. The treatment failed in a case associated with hypophysial nanism. Forty-three boys presented cryptorchism, which was unilateral in 3 cases. Five disappeared from control after having had three courses of roentgen irradiations, 29 were cured after three months of treatment and in 4 the testis descended before the first three months of treatment. The latter failed in 3 cases in adults. Results for the entire group were satisfactory, especially with regard to amenorrhea and cryptorchism.

Sperimentale, Florence

95:1-126 (March) 1941. **Partial Index**

*Liver in Chronic Tuberculous Enteritis: Anatomic and Microscopic Study. F. Parini.—p. 65.

Liver in Chronic Tuberculous Enteritis.—Parini reports a microscopic study of livers from 50 cadavers of patients dying from grave chronic ulcerative tuberculosis and from 50 dying from pulmonary and extrapulmonary tuberculosis without intestinal involvement. Cases of peritonitis, tuberculous lymphadenitis of the upper abdomen and tuberculous lesions of the pancreas or the spleen were excluded. He found fatty degeneration of the parenchyma of the liver of portal origin in all cases of ulcerative intestinal tuberculosis. It was selectively located at the periphery of the lobe in the areas supplied by the portal venules. The lesion occupied about one third of a lobe. In some cases, however, the entire lobe was involved by fatty degeneration with older lesions at the periphery. Fatty degeneration of the liver of portal origin paralleled the acuteness of the intestinal tuberculosis. In all cases of chronic intestinal tuberculosis but 13 peripheral fatty degeneration of the liver coexisted with some other alteration of the structure such as stasis in the hepatic venules in 8 cases, diffuse generalized miliary tuberculosis of the liver without miliary tuberculosis of other organs in 15 and with involvement of other organs in 5, interstitial miliary tuberculosis in 4 and early subacute interstitial hepatitis in 5. In the presence of stasis there are two zones of fatty degeneration, the perilobar caused by tubercle bacilli or their toxins by way of the portal vein, and the central due to stasis. Diffuse miliary tuberculosis of the liver without miliary tuberculosis of other structures is of portal origin and is to be differentiated from miliary tuberculosis of the liver of arterial origin. In the portal type the tubercles are minute, evenly distributed, recently formed and of a necrotic exudative type. The massive passage of tuberculous material from the intestine to the liver through the portal blood with consequent isolated miliary tuberculosis of the liver takes place only when the defense mechanism of the liver abruptly fails shortly before death. Chronic hepatitis of a sclerotic type does not complicate chronic intestinal tuberculosis the course of which is rapid. Death takes place before establishment of chronic disease of the liver.

Anales de la Facultad de Medicina de Montevideo

26:1-314 (Nos. 1-2-3-4) 1941. **Partial Index**

*Pigmented Secretions of the Breast Simulating Bleeding Breast. C. Stajano.—p. 243.

Pigmented Secretions of the Breast.—Stajano observed 20 cases of pigmented secretion of the breast simulating a bleeding breast and persistence for from six to fifteen years. The secretion increased near or after menstruation in some of the cases and was associated with premenstrual pain in others. Benign macroscopic or microscopic cysts existed in all. Cytologic examination of smears of secretions failed to show either fresh or modified erythrocytes. The secretions were negative for blood and hemoglobin, and positive for melanin. They contained large numbers of phagocytes and a few lymphocytes. They did not contain bacteria. The prognosis is good. Opotherapy is of no effect. The successful treatment consisted in improving the general resistance by administration of calcium, strychnine and arsenic. Involution following surgical castration brought about cessation of the secretion.

Deutsche Zeitschrift für Chirurgie, Berlin

253:435-562 (May 23) 1940

*Problem of Relationship Between Exophthalmic Goiter and Thymus. P. Sunder-Plassmann.—p. 435.
Aseptic Necrosis of Caput Femoris After Fracture of Neck of Femur in Young Persons and Its Relationship to Perthes' Disease. K. Bornebusch.—p. 458.
New Method for Surgical Collapse of Thorax: Suggestion for Operation. G. Tschmarke.—p. 472.
Etiology of So-Called Ileitis Terminalis Stenosans. A. Slany.—p. 495.
Chorionepithelioma in Man with Cutaneous Metastases. K. Rothmund.—p. 513.
Nailing of Medial Fracture of Neck of Femur. W. Heim—p. 523.
Operation for Cancer of Rectum. C. van Gelderen.—p. 540.
Possibility of Using Light Metals in Surgery (Metallic Magnesium as Stimulus for New Bone Formation). O. Maier.—p. 552.
Injury of Esophagus by Dull Force. R. Haecker.—p. 557.

Exophthalmic Goiter and Thymus.—Sunder-Plassmann states that he has come to realize through his own studies that some of the contradictions encountered in literature with regard to the role of the thymus in exophthalmic goiter are only apparent and in reality reflect different phases of a single biologic mechanism in the center of which is the thyroid, the thymus and the sympathetic and the parasympathetic with a special neurohormonal cell system. He had observed in thyroids of the newborn cell complexes with light nuclei which in his animal studies he had designated as neurohormonal cells. They are closely connected morphologically as well as functionally with the sympathetic portion of the vegetative nervous system. In dissecting the thyroid and the thymus of the newborn the author frequently observed narrow connections between the two. These connections appear as whitish, delicate formations which the author designated as the white "thymus street" of the thyroid. Serial sections of this structure reveal many large epithelioid cells with light nuclei. These neurohormonal cells represent a unique cell system controlled by the vegetative nervous system and connecting the thyroid and the thymus in a biologic complex mechanism. The thymus undergoes regressive changes, which commence when the thyroid is at the height of activity. The regression is characterized by the presence of a large number of Hassall's corpuscles and by the predominance of the lymphocytic cortex tissue. The medulla and cortex of the thymus seem to play entirely different roles. The medulla forms the epithelioid neurohormonal cells, which are largely dependent on the parasympathetic elements of the vegetative nervous system. The function of this neurohormonal cell system is the absorption of the colloid, thus providing the organism with thyroid secretion. The thymus cortex appears to have the function of fixing such colloid as is secreted too suddenly or in excessive quantities. It seems probable that the thymus serves chiefly the thyroid, with which it has close embryologic relationships. Further evidence of fixation of the thyroid secretion by the lymphocytic cortex of the thymus is offered by the occurrence of atrophy of the thymus after thyroidectomy and the fact that this atrophy can be transformed into hypertrophy, particularly affecting the thymic cortex, if thyroidectomized patients are fed thyroid extracts. The fact that the thymus may atrophy after prolonged activation of the thyroid, as well as in its complete absence, is only an apparent contradiction. In the delicately adjusted biologic mechanism of the neurohormonal thyroid-thymus system, manifestations of irritation, reactive changes and functional impairment may become manifest in the different and not always the same links of the chain and thus cannot be expected in all cases. Reactive changes in the thymus are closely connected with the activity of the thyroid and its effects in the organism. Adrenals and gonads probably play a secondary role in the neurohormonal thyroid-thymus system.

Klinische Wochenschrift, Berlin

20:33-64 (Jan. 11) 1941. **Partial Index**

Vitamin B_2 Content and Tissue Respiration in Brain. H. Leemann and E. Pichler.—p. 36.
Bone Regeneration. G. Levander.—p. 40.
*Comparative Tissue Thermometry. O. Lippross.—p. 49.
*Significance of Serum Heating Test for Diagnosis of Carcinoma. W. Zunke.—p. 53.

Comparative Tissue Thermometry.—Lippross discusses the technic of tissue thermometry and its superiority for diagnostic purposes over the usual skin thermometry. Tissue thermometry is done by means of an apparatus employing thermoneedles which are, preferably, thrust into the musculature of the calf of the leg and the ball of the hallus. (The lowest temperature in the tissues was found in the latter area; the highest [102.2 to 104 F.] in the liver.) "Comparative tissue thermometry" is defined as occurring when similar anatomic parts of the two lower extremities are measured simultaneously. Four punctures are required, which are said not to be particularly painful after some skill in applying the technic is attained. Single tissue tests, however, are often not sufficient. Tissue thermometry seeks (1) to ascertain whether pathologic conditions capable of thermometric determination exist at all and whether the index is higher in the calf than in the hallus area and (2) to institute special diagnostic tests in accordance with the temperature differences between the calf and the hallus index observed on the same side of the body. The author by this method was able to demonstrate especially low temperatures in the hallus ball tissue with serious circulatory disturbances in the toe joints of healthy persons of asthenic build. The subjective feeling of cold feet was rarely in keeping with objective measurements. Two cases will indicate the difference in accuracy between tissue and skin thermomeasurements. Sympathectomy performed for thromboangiitis obliterans showed, two months later, a 1.5 C. higher skin temperature in the affected limb. Two years later no difference was observed on the two sides. Tissue thermometry, however, disclosed a difference of from 5 to 6 C. in the hallus ball area. In a case of intermittent claudication lasting ten years sympathectomy was contraindicated because no comparative difference in the skin temperature on the two sides could be observed. Tissue thermometry, however, disclosed a considerable regulatory dysfunction in one member. Thermometric tests included cold and hot baths, with the legs kept out of the water to permit uninterrupted tissue examination. The author believes that this technic represents progress in the functional diagnosis of pathologic conditions in the lower extremities. More deeply situated tissue is not subject to numerous external factors, hence permits a more exact measurement and affords a better understanding of the regulatory processes of the body. This technic makes possible not only the progressive measurement of the temperature of the different tissues and their fluctuation under certain circumstances but also the simultaneous measurement of the temperatures of these tissues.

Serum Heating Test for Diagnosis of Carcinoma.—Zunke employed Kürten's technic for the detection of carcinoma in 531 cases involving 891 double tests and retests. According to Kürten, when 1 cc. of human blood serum is slowly heated over a burner in a small test tube, two reactions will occur: either (type I) the albumins will precipitate and adhere to the sides of the tube, at the same time releasing an opalescent fatty salt solution, or (type II) the total serum will coagulate and remain in this condition in spite of continued heating. The first reaction characterizes predominantly the serums of healthy as well as ill persons. The second is found in the serums of subjects with malignant tumors and in some cases of acute and chronic disease. However, Kürten found that on the subsidence of the acute stage the serum would give a type I reaction. In 492 of 531 of Zunke's serum specimens, heating tests and retests confirmed clinical or postmortem diagnosis. In the remaining cases, operation or necropsy could not be performed or the patients could not be observed long enough. Forty-six cases involved carcinoma. Coagulation type I in these was observed only four times, all in patients previously roentgenologically treated. Four hundred and thirty-seven were nontumor cases; 43 of these, the majority pneumonia (15), showed type II reaction. Lobar pneumonia invariably gave a type II reaction in the acute stage and a type I reaction during subsidence. Like Kürten, Zunke found that the serum of carcinomatous subjects and those affected with certain acute and chronic diseases presented a type II coagulation. The diagnostic value of

the serum test was not impaired when clotted or centrifugated serum, refrigerated for a few days, was used; hemolytic serum, however, proved unreliable. The author believes that Kürten's technic employed routinely may be of value in discovering the possible presence of carcinoma, especially in cases in which more complicated cancer examinations are in order. The technic, simple as it is, needs to be carried out with the greatest care. Otherwise the results will be vitiated.

Münchener medizinische Wochenschrift, Munich

88:117-148 (Jan. 31) 1941. **Partial Index**

*The Problem of Carcinoma. W. Brünings.—p. 117.
Frostbites. F. Bering.—p. 123.
Food Poisoning by Means of Duck Eggs. H. Müller.—p. 125.
Albers-Schönberg Marble Bone Diseases. H. Kramer.—p. 132.

Problem of Carcinoma.—Brünings, working on the theory that neuroendocrine disturbances of the carbohydrate metabolism may be etiologically involved in carcinoma, attacked the problem by combining a dietary regimen poor in carbohydrates with insulin therapy in 14 cases of nasolaryngologic cancer, only 1 of which was associated with diabetes. The carcinomas selected were those in hopeless cases but susceptible of being viewed, together with their metastatic invasion of the lymph nodes, macroscopically and the tissues of which could be excised for microscopic study. In all cases, general as well as local, amelioration was temporarily observed, varying from arrest of tumor growth to total macroscopic disappearance of the tumor and its metastases. Body weight invariably increased in the first weeks, slowly falling after from one to two months but rarely below initial levels. This improvement lasted from two to three months, after which a reactivation of tumor growth set in and a tendency to necrosis, pain and hemorrhages. Further treatments were unavailing. Under the microscope, in most cases, the reduction of malignant growth turned out to be only a quantitative diminution; excised tumor portions showed degenerate cancer cells. No essential modification of insulin tolerance was observed, nor subjective or objective damage due to hypoglycemia. The tolerance limits varied considerably in different persons. If primary tumor did not promptly respond to the therapy, roentgen irradiation was at once instituted. In 2 cases in which the combined treatments had already clearly brought about tumor recession, it was noted that on withdrawal of the insulin the malignant condition was stimulated to new life or that the tumor-retarding protection had ceased. The same observations were made in 2 other cases in which only the diet had been administered for ten days. Even a combined therapy in which insulin dosage was pushed to the individual limits of tolerance yielded no information as to the effect of insulin, or of any unknown factor in insulin, on carcinoma. The author believes that a causal connection exists between carcinoma and carbohydrate metabolism which needs to be further investigated. The favorable results temporarily obtained lead him to think that combined dietary and endocrine treatments may be of value in aiding diagnosis when carcinoma is suspected, in conditioning the patient for an operation to be performed and as an adjuvant of roentgen therapy.

Nervenarzt, Berlin

13:337-384 (Aug. 15) 1940

Geography of Suicide. H. W. Gruhle.—p. 337.
*Postoperative Reduction of Intracranial Pressure After Brain Operations: Pathophysiology of Cerebrospinal Fluid System. H. Sprockhoff.—p. 341.
Percutaneous Arteriography. P. Duus and W. Behrmann.—p. 350.
Differential Diagnosis of Pathologic Changes of Sella Turcica in Roentgenogram. H. Greving.—p. 353.
*Cerebrospinal Fluid in Multiple Sclerosis. O. Seuberling.—p. 359.

Intracranial Pressure After Brain Operations.—Sprockhoff points out that, in some patients who have undergone surgical intervention on the brain, the formation of cerebrospinal fluid does not keep pace with the resorption, and the result is deficiency and hypotension of the fluid. He lists 11 cases in which there was such postoperative hypotension. With the exception of 2 patients who had undergone removal of the squama occipitalis, all had supratentorial defects of the cranium. The patients have headache and are restless and irritable before the hypotensive state develops. The sensorium becomes dulled; slight rigidity of the neck, fatigue, lassitude and nausea develop. There usually is a mild hyperthermia and hyperpnea, but the blood pressure and the pulse remain normal. Pallor is occasionally seen. If there is a cranial defect, retraction is noticeable. The pupils become rigid, and reflexes abolished. Respiration becomes snoring and approaches the Cheyne-Stokes type. This comatose condition may also develop without the prodromal signs. The hypotensive condition does not always lead to complete coma. Differentiation from increased intracranial pressure (brain swelling arachnoiditis) may be difficult, particularly if there is no cranial defect. The proof that the described clinical symptoms are produced by hypotension in the fluid space is furnished by the fact that intraspinal administration of physiologic solution of sodium chloride promptly counteracts the acute symptoms. If too much fluid is introduced, the skin over the cranial defect will bulge and the undesirable tension may have to be counteracted by another puncture. On the other hand, the retraction in the defect may recur after the filling so that intraspinal injection has to be repeated. This instability shows that the lack of fluid is not the only cause but that there is also a disturbance in the dynamic equilibrium between formation and absorption of the cerebrospinal fluid. For this reason filling of the fluid space is not sufficient. As few punctures as possible should be made, because every puncture that is not required to counteract acute hypotension or excess pressure retards the regulation. It is necessary to aid the organism in maintaining normal pressure. Fluid should be given in generous quantities; in the mild cases by mouth, in the severe cases by intravenous infusion of sodium chloride or dextrose solutions. The author supported the oral administration of fluid with caffeine in order to increase the blood perfusion of the choroid plexus and thereby stimulate the production of the cerebrospinal fluid. Since erect posture promotes absorption of the cerebrospinal fluid and favors decrease in pressure, this posture should be avoided in hypotension, contrary to the general rule in postoperative treatment. Patients with hypotensive conditions complain of headaches which do not differ from those caused by increased intracranial pressure except that they cannot be improved by the withdrawal of spinal fluid but require intraspinal administration of fluid. The prolonged headaches complained of after lumbar puncture by psychopathic persons or by those with weak sympathetic nervous systems are probably of this hypotensive type. Two of the author's patients had chronic hypotensive symptoms, suffering for years with severe headaches. Both had considerable defects in the cranium and, having noticed that greater severity of headaches was accompanied by greater retraction, they requested plastic repair, after which they were free from complaints. Reduced secretion is the decisive factor, and this in turn must be due to impairment of the plexus. Various causes, such as senile involution, diffuse atrophy of the brain, prolonged existence of internal hydrocephalus, reduced blood pressure and general exsiccation may be responsible. The author points out that some employ an exsiccating preoperative treatment in order to avoid postoperative swelling of the brain. This preoperative exsiccation proved its value. The author does not reject the method but emphasizes that it should be used with discrimination, for, if it is employed in all cases, postoperative hypotension will be more frequent. It should not be employed in cases in which the previous history or clinical aspects indicate a tendency to hypotension.

Cerebrospinal Fluid in Multiple Sclerosis.—Seuberling reports the serologic picture of cerebrospinal fluid in 140 cases of multiple sclerosis observed at the neurologic clinic of the university of Würzburg. The results obtained, together with those of three other German clinics, suggest that the cerebrospinal fluid of 75 per cent of patients with definitely established multiple sclerosis shows pathologic changes. The author was

able to corroborate the observation of several other investigators that a correlation exists between changes in the cerebrospinal fluid and severity of the multiple sclerosis. Pathologic alterations of the cerebrospinal fluid occurred twice as frequently in patients with severe multiple sclerosis as in those with a mild form. During the acute attack only 2 per cent of the fluids were normal. The largest percentage of normal fluids was obtained from patients whose disease had lasted less than a year. In the course of the first attack 98 per cent of the patients show pathologic changes in the cerebrospinal fluid, but in more than one half of these the fluid becomes normal later on. In patients with chronic multiple sclerosis the fluid is much less likely to become normal after an exacerbation. Efforts have been made at the author's clinic to develop a specific reaction for multiple sclerosis by paying particular attention to the lipoid metabolism and the lipolytic ferments in the cerebrospinal fluid. No characteristic sign or behavior has thus far been detected. Spinal punctures have not been found harmful at the author's clinic except for occasional retention of urine for about a day. Punctures should not be made in cases of multiple sclerosis in which foci are suspected to exist on the floor of the fourth ventricle and in which bulbar and vagal symptoms appear. The author observed a coma of several days' duration following a puncture in a case of this type.

Zeitschrift für Kinderheilkunde, Berlin

62:1-110 (Aug. 9) 1940

Disturbance of Cysteine-Cystine Metabolism in Young Children and Its Relation to Dwarfism and Renal Rickets. H.-D. Pache.—p. 1.
Congenital Erythroblastoses. J. Hattler.—p. 16.
*Therapeutic Success of Three Different Treatments of Epidemic Meningitis. H. Boehncke.—p. 29.
Study of Phosphorus Metabolism in Congenital Athyreosis. B. Breitbarth.—p. 52.
Modification of Blood Composition in Toxic Forms of Diphtheria, Scarlet Fever, Dysentery and Endocarditis by Desoxicorticosterone Acetate. W. Semmann.—p. 65.
Incidence, Course and Treatment of Primary Tuberculosis of School Children and Adolescents. A. Viethen.—p. 80.
Connection Between Sclerodermia and Progeria. B. Müller-Hess.—p. 96.
*Can Skimmed Milk Be Rendered Antirachitic by Irradiation? K. Scheer. —p. 104.

Therapy of Epidemic Meningitis.—Boehncke compares 44 cases of epidemic meningitis in which serum therapy was employed with 46 in which serum and a sulfanilamide preparation were used. There were 30 fatalities among those treated with serum, a mortality of 68 per cent. In the 46 cases treated since 1938 in which a sulfanilamide preparation was given in addition to the serum, the mortality rate was reduced to 8.6 per cent. Although the two groups were treated in different periods and the age distribution was slightly different, the author thinks that this does not explain the difference in the mortality rates. The sulfanilamide preparations used were prontosil album and albucid (= acetylsulfanilamide). Sulfanilamide was given in the first 20 of the 46 cases and acetylsulfanilamide in the other 26. The author prefers the latter preparation because it can be given in concentrated solution by intravenous, intramuscular and intraspinal injection and because its toxicity is less than that of sulfanilamide. Another advantage of acetylsulfanilamide especially important in meningitis is that it readily passes the cerebrospinal barrier. Acetylsulfanilamide proved more effective. Of the 20 cases in which serum and sulfanilamide was used, 4 had a fatal outcome, whereas among the 26 treated with serum plus acetylsulfanilamide there were no fatalities. The author concludes that the treatment with meningococcus serum plus acetylsulfanilamide is the method of choice in epidemic meningitis.

Irradiation of Skimmed Milk.—Scheer points out that a considerable portion of the total cholesterol content of milk is combined with the proteins, particularly lactalbumin. He deduces that the antirachitic power of irradiated milk is not limited to its fat content. Thus it seemed of interest to determine whether skimmed milk can be rendered antirachitic by irradiation. From comparative experiments with irradiated whole milk and irradiated skimmed milk he learned that irradiated skimmed milk has an antirachitic action which will cure a severe florid rickets, although the time required for such cure is somewhat longer than with the use of irradiated whole milk.

Bulletin of the Naval Medical Association, Tokyo

30:137-196 (March 15) 1941. **Partial Index**

*Prophylaxis for Diphtheria Among Navy Men. K. Kariya, K. Yamamoto and T. Shibatani.—p. 137.
*Report of Necropsy on Pellagra. M. Nakamura, C. Hamada and H. Oriuchi.—p. 179.

Diphtheria Prophylaxis for Sailors.—Kariya and his associates found positive Schick reactions in 5 per cent of the entire crew below the rank of noncommissioned officers on a cruiser. After ascertaining the probable freedom from sensitivity by means of the Moloney test in these Schick-positive reactors, they administered a total of diphtheria anatoxin varying from 1.1 to 1.5 cc. in three divided doses at weekly intervals (0.2, 0.5 and 0.8 cc.). From careful statistical observations as to the incidence of diphtheria as well as of acute tonsillitis and acute laryngopharyngitis on the ship, the authors found diphtheria to have been completely eliminated and acute tonsillitis and pharyngitis greatly reduced among these men during the twelve months following the prophylactic immunization. Schick tests then repeated on these men gave, without exception, negative reactions. From these results it is recommended that diphtheria anatoxin, in the amount of 1.5 cc. and administered in three divided doses at weekly intervals, be employed as an effective measure in the prophylaxis of diphtheria.

Pathology of Pellagra.—Nakamura and his associates give a detailed report on the necropsy in a case of pellagra occurring in a sailor with a history of chronic gastrointestinal disturbance. The patient had complained of vague epigastric pain, numbness of the lower extremities and slight edema, all suggestive of beriberi. The roentgenogram revealed a mild degree of gastroptosis, and the gastric acidity was extremely low. Except for a slight leukocytosis with a left shift, blood counts and serologic tests were essentially negative. Urinalysis showed the presence of albumin and urobilinogen. After a slight improvement the patient was allowed to go fishing at the hospital lagoon, and the sunlight to which he was thus exposed caused his skin to become erythematous with the development of a tingling sensation; later the skin became brownish with a bran-like desquamation. These cutaneous lesions failed to clear up and turned into well demarcated copper hued areas in the middle of the chest, on the nose, and over the knees and dorsum of both feet. Urinalysis at this time revealed the presence of indican in addition to urobilinogen. Administration of high dosage of vitamins B_1 and B_2 failed to produce improvement. Necropsy revealed marked atrophy of the heart, kidneys, liver and intestine, excessive dilatation of the stomach with evidence of atrophic gastritis, and numerous hemorrhages in the entire gastrointestinal tract. There was definite scar formation in the pachymeninges as well as in the leptomeninges of the frontal lobe, together with a considerable degree of round cell infiltration. Microscopically the myocardium was greatly atrophied and the liver also generally atrophic with fibrosis of Glisson's capsule and cellular infiltration. The muscle fibers near the pylorus of the stomach were slightly hypertrophic with round cell infiltration in the interstitial spaces, most pronounced near the nerve fibers. A few Russell's bodies were seen in the mucosa, which was highly atrophic. The intestinal mucosa was also atrophic and the follicles were increased in number, with evidence of extravasation of blood around the capillaries.

Tokyo Igakkwai Zassi, Tokyo

55:189-274 (March) 1941. **Partial Index**

*Studies on the Function of Hypophysis in Carbohydrate Metabolism. T. Sakai.—p. 189.

Hypophysis in Carbohydrate Metabolism.—Sakai started his investigations on the function of the hypophysis in carbohydrate metabolism by first observing sugar assimilation in 14 cases of acromegaly, in 64.3 per cent of which he found glycosuria. In over half of these cases the glycosuria was found to be renal in nature, with a spontaneous and markedly fluctuat-

ing elevation of the excretory threshold. In all cases in which glycosuria was present the duration of the disease had been more than ten years. In only 3 cases was there fasting hyperglycemia, with a definite lowering of sugar tolerance. Sakai believes that hyperglycemia in acromegaly is extrainsular in origin. The second phase of his studies deals with the observations of sugar metabolism in patients with disturbance in the anterior pituitary lobe. Of 9 cases of dwarfism, 4 cases of cachexia, 3 cases of polyglandular deficiency, 2 cases of eunuchoidism and 3 cases of dystrophia adiposogenitalis the majority exhibited disturbances in sugar metabolism, such as delayed restoration of normal blood sugar level following alimentary hyperglycemia, slow development of epinephrine hyperglycemia, glycosuria and reelevation of both sugar tolerance and the excretory threshold. In a further study of sugar metabolism in 6 cases of diabetes insipidus the author found practically no evidence of disturbed sugar metabolism. In 10 cases of hypophysial dysfunction without association of endocrine disturbance, Sakai found 2 patients presenting symptoms of anterior lobe dysfunction during pregnancy with renal glycosuria, which he explained on the basis of the pregnancy-cell-nodule hypothesis of Erdheim. In the experimental animal (rabbit) the author saw an immediate elevation of the sugar excretion threshold by the intravenous or subcutaneous injection of gonadotropic extract from pregnancy urine. One or one and a half months after the subcutaneous injection the threshold was gradually lowered, and repeated administrations at this stage no longer produced reelevation. Identical results were obtained with a similar injection of adrenal cortex extract. These observations prove that elevation of the renal threshold produces marked alimentary hyperglycemia and that the metabolic function is at its best when the renal threshold is low.

Acta Chirurgica Scandinavica, Stockholm

84:383-478 (March 29) 1941

Operation for Carcinoma of Rectum per Laparotomiam with Conservation of the Anal Portion. A. Troell.—p. 383.
Subcutaneous Total Rupture of Achilles Tendon and Its Treatment. N. Silfverskiöld.—p. 393.
Is Urography a Reliable and Valuable Differential Diagnostic Aid in Acute Appendicitis? H. B. Wulff.—p. 414.
*Serotherapy in Peritonitis. G. Bohmansson and E. B. Norup.—p. 427.
Pathology and Clinical Aspects of Papillitis Necroticans Renalis. J. Mellgren and G. Redell.—p. 439.
Simplified Method of Extraoral Trunk Anesthesia of Second and Third Branch of Trigeminus and of Gasserian Ganglion. J. Quittner.—p. 458.
Benign Ureteral Tumors. T. Olovson.—p. 469.

Serotherapy in Peritonitis.—Bohmansson and Norup state that acute septic perforation peritonitis has been treated at their hospital in Oerebro with serum since 1934. In 1935 one of them reported at a meeting in Copenhagen that until then serotherapy had not reduced the mortality of peritonitis. On the basis of subsequent observations, however, they arrived at a different conclusion. They found that as long as small doses were used, namely from 20 to 40 cc., the mortality did not decrease. During the ten year period from 1929 to 1938 the mortality was above 40 per cent. The authors restrict the term diffuse septic peritonitis to cases which show a much impaired general condition, diffuse abdominal tenderness, peripheral circulatory disturbances, severe impairment of the intestinal function and free purulent exudate in the abdomen either of putrid odor or yielding bacteria by culture, the culture being made immediately after opening of the abdomen, before the focus is touched or exploration has been done. Only cases which fulfilled all these requirements have been counted, and this explains the high mortality. During 1939 and 1940 the authors used much larger doses of serum. They now introduce at the time of operation 60 cc. into the abdomen and 40 cc. intravenously, and in exceptional cases supplementary doses are given on the following days. This serum therapy was combined with sulfanilamide medication, which is continued for from four to five days. In this way it was possible to reduce the mortality to 6.3 per cent. The material on which the present report is based comprises 3,787 cases of gangrenous appendicitis, of which 626 had perforated before the operation and 210 cases were complicated with diffuse septic peritonitis. The authors conclude that with large doses of serum combined with sulfanilamide it will be possible to lower the mortality in diffuse peritonitis but that this treatment is of no particular value in circumscribed peritonitis. Anaphylactic shock is rare with these large doses not only when administered under general anesthesia in the course of operation but when given under spinal anesthesia as well.

Acta Medica Scandinavica, Stockholm

106:239-344 (Feb. 17) 1941

Nature of Certain Peculiar Corpuscles Present in Tissue of Lymphogranulomatosis Benigna. J. Schaumann.—p. 239.
Plasma Protein in the Epileptic During Inanition. R. Eeg-Olofsson.—p. 254.
Excretion of Fluorine in Urine in Chronic Fluorine Poisoning in Workers with Kryolith. G. C. Brun, H. Buchwald and K. Roholm.—p. 261.
*Experimental Studies on Production of Pernicious Anemia by Operation on Digestive Tract: Survey of Results of Total Gastrectomy and Resections of Stomach. S. Petri and H. Jensenius.—p. 274.
Population and Clinical Statistics of Pulmonary Infections. J. Rudebeck.—p. 293.
Acute, Nonfatal Cocaine Poisoning: Four Cases. N. Alwall.—p. 335.

Production of Pernicious Anemia.—Petri and Jensenius review results of other investigators and their own on the operative measures carried out on the stomach in an attempt to produce pernicious anemia. Various anemic conditions (depending on the species of animal and the type of operation) have developed but in none of the many experiments has pernicious anemia been produced successfully, with the simultaneous appearance of the typical characteristics: hyperchromic megalocytic anemia, hyperplasia of the bone marrow and capacity for reaction to liver therapy. Nor has this been accomplished after toxic or other injurious treatment of the animals operated on. In a few cases a blood picture resembling pernicious anemia has been observed. In gastrectomized pigs a severe chronic and finally fatal pellagra has appeared. The condition also appeared in other species submitted to such treatment. The frequency with which spontaneous anemias have appeared in the dog has varied somewhat: after total gastrectomy in 78 per cent, after subtotal gastrectomy or resection of the stomach in 59 per cent and after "isolation of the stomach" in only 27 per cent. In contrast to this, after resection of the fundus or pylorus, anemia developed in 100 per cent of the cases. The less frequent occurrence of anemia when the stomach was made to form a closed pocket suggests the hypothesis advanced by Morris and his collaborators (1933): that the stomach might have some endocrine substance with an antianemic function. In dogs, swine and rats, the more common types of anemia have been hypochromic anemia (most frequent) and "isolated hypochromia." In the monkey only hypochromic anemia has been diagnosed. There is some difference in the time it takes anemia to develop after various operations. Animals seem to become anemic more rapidly after total gastrectomy and resection of the fundus than after resection of two thirds of the stomach. Accordingly removal of the fundus area may possibly prove most decisive for the development of the anemia. In dogs remission has been observed especially after resection of the fundus and in swine only after resection of the pylorus. The authors discuss the views concerning the failure to produce pernicious anemia experimentally by operations on the stomach. The views have varied owing to the variable stand of the clinicians with regard to the antipernicious anemic activity exerted by various parts of the digestive tract and also reflecting in part the uncertainty which recently has asserted itself with regard to the site and mode of formation of the active liver principle. Before the studies are extended further the authors believe that the biologic foundation for a positive result must be cleared up. They conclude that since the operations used so far have not resulted in pernicious anemia—despite the fact that animals appear to possess the biologic foundation for such a condition—two possible causes suggest themselves: (1) either the site of formation of the intrinsic factor is not interfered with sufficiently by the operation or (2) the correctness of Castle's theory has to be questioned.

Book Notices

Essentials of Dermatology. By Norman Tobias, M.D., Senior Instructor in Dermatology, St. Louis University, St. Louis. Cloth. Price, $4.75. Pp. 497, with 143 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1941.

Tobias presents an excellent compact synopsis on dermatology in which, "as far as practical, each disease is discussed from the standpoint of internal medicine." The subject matter of the book is divided into thirty sections, e. g. the erythema group, the eczema group, drug eruptions, the toxic bullous diseases, diseases due to physical agents, diseases due to psychic and nervous disorders, tuberculosis of the skin, the deep infective dermatoses, syphilis and malignant growths of the skin, the metabolic disorders, pigmentations, the lymphoblastomas, the erythrodermias and a section on dermatologic therapeutics. All the subjects are discussed well in a succinct manner with a good literary style. Under metabolic dermatoses the avitaminoses are discussed. The accepted newer concepts in dermatology are incorporated in the discussions in the book. In the first section, on basic survey, under etiologic factors the author discusses atopy and nonatopic allergy together with drug, bacterial and physical allergy. Under diagnostic methods he mentions briefly those important pertinent procedures of interest to dermatologists and to the practitioner interested in diagnosis in dermatology. In this section there is also an excellent discourse on the cutaneous manifestations of systemic disease. There are one hundred and thirty-eight halftone illustrations of dermatoses, of good quality. The book is in convenient small form printed on good paper with a clear legible type and is an excellent addition to the compact textbooks dealing with the essentials of dermatology and should have a place in the library of students and general practitioners who desire to acquaint themselves with the basic facts of dermatology.

Sex Variants: A Study of Homosexual Patterns. By George W. Henry, M.D. With Sections Contributed by Specialists in Particular Fields. Volumes I and II. Sponsored by Committee for the Study of Sex Variants, Inc. Cloth. Price, $12.50, per set. Pp. 546; 549-1179, with 66 illustrations. New York & London: Paul B. Hoeber, Inc., 1941.

In 1935 a committee was established to study sex variants. The membership included some of the most distinguished workers in this field, associated with experts in biology, psychiatry, genetics and similar subjects. Arrangements were made to secure interviews with a considerable number of persons known to be homosexual, and in these two volumes are reported a complete study of 80 persons of this type. For each there is a genetic chart, a record of general impressions, the family background, the personal history, the physical examination, including a special study of the sex characteristics, and a complete roentgenologic study, then a comment and a summary.

At the end of the second volume there appear a number of collected studies. The author is convinced that the sex variant is a by-product of our civilization—an expression of inability to meet the responsibility of establishing and maintaining a home which involves the rearing of children. Unfortunately, investigations made in primitive civilizations seem to indicate that in such instances as well the sex variant is not infrequent.

An interesting observation is the following: "All persons who manifest violent emotional reactions to the sex variant warrant serious consideration. Such persons may be reacting to personal experience or they may be on the defensive lest they disclose their own unconventional desires and impulses."

Another significant conclusion is the following: "There is no adequate substitute for well adjusted parents. The supervision of the psychosexual development and conduct of children is one of the greatest responsibilities of parenthood. Servants, siblings and other relatives as well as friends often contribute to the psychosexual distortion of children. In our present state of ignorance regarding sexual matters, a parent who is fully prepared to undertake the responsibility of supervising the psychosexual development of his children is a rare person."

There are altogether five and one-half pages of these impressions, which should be read with care by every one who may be concerned with this problem. It is indicated that the law has been a conspicuous failure in handling this serious situation. Society has no solution for the problem. Scientific approach would seem to be the only answer.

Special supplements to the book include a series of masculinity-femininity tests of men and women, some full page illustrations of physical characteristics, scientific studies of roentgen anthropometry, a gynecologic study by Dr. Dickinson and a series of drawings, and finally a study of the language and vocabulary of sex variants.

The book is a most useful scientific contribution to the subject, obviously to be restricted in its distribution to those with a legitimate scientific interest.

A Manual of Maladies Influenced by Oxalic Acid Poisoning viz. Industrial Myositis Fibrosa, Occupational Schizophrenia and Experimental Wassermann and Kahn Tests. By Abel C. Anthony, B.S., M.D. Cloth. Price, $2. Pp. 85, with 17 illustrations. Chicago: The Author, 1941.

The temptation is to label this badly printed booklet both as confused and as confusing. These things this book is, but deep within its shortcomings there may be some fundamental disclosures warranting more careful inquiry. The book holds and claims to prove that oxalic acid is one cause of myositis fibrosa, is in some instances a specific cause of schizophrenia and that the presence of oxalic acid in the body upsets the diagnostic serologic reaction to the point that faulty diagnoses of syphilis are made. The author's material chiefly is derived from workers of a public carrier company in Chicago, where oxalic acid was one constituent of a cleaning fluid for toilet fixtures, cuspidors and wash basins. The author's arguments are colored by unveiled antipathy for the employer and the medical activities of the staff of an unnamed hospital designated as "carrier elected hospital." He provides no quantitative evidence as to exposures either for his patients or for experimental animals. The diagnosis of industrial oxalic acid poisoning apparently rests on qualitative exposure plus the presence of quantities of oxalate in the urine, blood and certain tissues. Anthony does not overlook the fact that normal urine may contain in the daily output from 30 to 40 mg. of oxalic acid (oxalates?) and that this amount may be augmented by a diet that includes rhubarb, tomatoes, asparagus, spinach or sorrel. He however possibly overlooks or minimizes the fact that oxalate crystals may be demonstrated in some normal tissues at all times.

Despite the author's concepts of scientific possibilities from oxalic acid poisoning, his evidence distressingly defeats his objectives. For example, at one point it is set forth that the minimum lethal dose for human beings is 60 grains, but at one point the author in presenting a finding of 0.275 mg. of oxalic acid in a 140 mg. forearm biopsy specimen taken from a 140 pound woman has furnished basis for the calculation that if the oxalic acid was equally distributed over the body at that moment there must have been a total body content of 1,947 grains. By all the rules this patient should have been dead some years earlier, since apparently the last exposure to oxalic acid was more than two years earlier.

Diseases of the Digestive System: A Text-Book for Students and Practitioners. By Eugene Rosenthal, M.D., Lecturer in the Medical Faculty, Royal Peter Pázmány University, Budapest, Hungary. With a preface by R. J. V. Pulvertaft, M.D., F.R.C.P., Reader in Pathology, University of London, London. Cloth. Price, $8.50. Pp. 394, with 234 illustrations. St. Louis: C. V. Mosby Company, 1940.

This is a rather unusual book. It is essentially an eclectic presentation of lectures on the digestive system and a mass experiment in mnemonics. It is difficult to evaluate the lavish use of color and geometric design of the author's diagrammatic attempts to fix signs, symptoms and their association for the reader. Undoubtedly this method of presentation was developed by years of teaching experience. Whether it will have the same value in a textbook as it had in the class room can be decided only by the reader. The text is divided into five chapters covering diseases of the esophagus, diseases of the stomach and intestinal tract, diseases of the liver and biliary tract, diseases of the pancreas and diseases of the peritoneum. The material is not an epitomized version of a textbook on this subject. It apparently represents the author's rich clinical experience carefully organized and dogmatized for effective presentation. The author's style is simple and practical. Pathology, diagnosis and treatment are concisely but

effectively presented. The frequent use of colored diagrams, charts and roentgenograms is a distinct aid to the reader in fixing the factual data. This is a book that the physician can profitably purchase though he may possess other textbooks on the digestive system. It is a painstaking effort by a trained clinician and teacher.

Common Mistakes of Surgery in India and How to Avoid These: A Practical Handbook for the Young Surgeon, the General Practitioner, the Hospital Medical Officer and the Surgically Minded Student. By Lt. Col. A. N. Palit, O.B.E., F.R.C.S., M.R.C.O.G., Senior Surgeon, Chittaranjan Seva Sadan Hospital, Calcutta. Cloth. Price, $3. Pp. 382, with illustrations. Calcutta: Book Company, 1940.

The common mistakes of surgery in India and modern surgical practice are discussed in this book, written by a civil surgeon who has had long experience in Bihar and Orissa. It contains chapters on anesthesia in Indian practice, antiseptics, fractures and joint injuries, head injuries and cranial surgery, eye, ear, nose and throat, abdominal injuries and operations, rectal and genitourinary surgery, gynecology and modern treatment with sulfonamides and its abuses. The field of surgery appears to be covered extensively, giving the various methods of treatment and the author's views and knowledge gained through eminent surgeons who were his teachers. The book has been written for the general practitioner, the physician in charge of a small hospital, the young surgeon and the student interested in surgery. The style of the book, however, is poor and many words are misspelled.

Getting Ready to Be a Mother. By Carolyn Conant Van Blarcom. Revised by Hazel Corbin, General Director Maternity Center Association, New York. Fourth edition. Cloth. Price, $2.50. Pp. 190, with 90 illustrations. New York: Macmillan Company, 1940.

The general practitioner, the obstetrician and the pediatrician often may find it advantageous to have a mother familiarize herself with the principles of conduct during and after pregnancy. This book may be recommended with confidence for this purpose. It should aid mothers materially in carrying out the physician's recommendations during pregnancy and in managing the infant during the important early weeks. As is true with many such books, certain ideas are advanced which may differ in point of view from those generally accepted, but these are presented only occasionally. For example, the suggested method of administering cod liver oil is not that which is generally approved. The makeup of the book is excellent and the illustrations are more than satisfactory; the book is clear, simple and interesting.

Hutchison's Food and the Principles of Dietetics. Revised by V. H. Mottram, M.A., Professor of Physiology at King's College of Household and Social Science, University of London, and George Graham, M.D., F.R.C.P., Physician to St. Bartholomew's Hospital, London. Ninth edition. Cloth. Price, $6.75. Pp. 648, with 30 illustrations. Baltimore: William Wood & Company, 1940.

This book first appeared in 1900. The present edition indicates better than words its past value and usefulness to physicians and others interested in dietetics. The present editors realize that there is now little need for an encyclopedic book on dietetics which lists table after table of nutritive values of innumerable foods and that the emphasis now is on the "newer knowledge" of nutrition. From these two points of view, Mottram and Graham have extensively revised or in many instances completely rewritten the chapters, which have been rearranged into four sections: diet in normal life, the nature of foods, the principles of feeding in infancy and childhood, and diet in the treatment of disease. This revision brings this classic book on dietetics to be an authoritative expression of that which is both old and new. It should prove to be a useful book for daily reference by all interested in nutrition.

Les syndromes douloureux de la région épigastrique. Par René A. Gutmann, médecin des hôpitaux de Paris. Préface du Professeur A. Gosset. Tomes I et II. Third edition. Paper. Price, 495 francs. Pp. 750; 737, with 316 illustrations. Paris: G. Doin & Cie, 1940.

These two volumes compose an exhaustive treatise on maladies affecting the epigastric region. (The pancreas is included in a separate volume.) The work is richly illustrated with nine hundred and three roentgenograms and four hundred and thirteen diagrams. Emphasis is placed on the importance of detailed, accurate history taking and thorough physical examination as aids to exact diagnosis. Contents include discussion of ulcers of the stomach and duodenum, cancer and gallbladder disorders. The perivisceral syndromes, dyspepsias (allergic, menstrual, nervous), hemorrhages, gastritis and duodenitis, avitaminosis, gastric crisis and malformations of the diaphragm and stomach also are discussed. Treatment is outlined in each section. This treatise should be useful to internists who read French. The sections on gastroscopy are limited. In general, however, there is a wealth of detail. The major criticism of the book is its length. The emphasis, from the diagnostic point of view, is far more detailed than the usual American work on gastroenterology. Some of the newer fields, as avitaminoses and gastrointestinal allergy, are treated at length.

Die Bakteriologie der Salmonella-Gruppe. (Typhus-Paratyphus-Enteritis-Gruppe). Von F. Kauffmann, Abteilungsleiter am Staatlichen Seruminstitut Kopenhagen. Paper. Price, 29 Danish kroner. Pp. 393. Copenhagen: Einar Munksgaard, 1941.

The Salmonella or paratyphoid group of bacteria has been studied extensively by Bruce White in England and by Kauffmann in Copenhagen. By means of the agglutinin absorption test these strains have been studied and classified. The number of antigens in a given specific species may be many and thus the antigenic components of the group as a whole form a complex mosaic pattern. At the State Serum Institute in Copenhagen an international Salmonella center has been established and financed by the Commonwealth Fund. This center will supply gratis to national Salmonella centers in various countries all serums and cultures necessary for serologic diagnosis. Furthermore the international Salmonella center in Copenhagen is prepared to examine doubtful cultures without charge. Kauffmann has brought up to date in this report the more recent developments in this field. This book can be recommended to laboratory workers who are attempting to classify strains of Salmonella or to bacteriologists engaged in this field of research.

The Pharmacology of Anesthetic Drugs: A Syllabus for Students and Clinicians. By John Adriani, M.D., Instructor in Anesthesia, New York University College of Medicine, New York. Second edition. Fabrikoid. Price, $3.50. Pp. 86, with illustrations. Springfield, Illinois & Baltimore: Charles C. Thomas, Publisher, 1941.

The pharmacology of anesthetic drugs is displayed in a unique fashion, making possible brevity with relative completeness. The author has based his statements either on experience or on statements that are considered not to be controversial that have been published elsewhere. The useful items of interest are included in the briefest possible form, such as a glossary, a bibliography and formulas of drugs, together with some laboratory results which fortify the statements as to clinical results. It is a book which those interested in anesthetic drugs will find valuable to have at hand for reference or for a quick review of the action of anesthetic drugs.

Counseling the Handicapped: A Manual on Aptitudes and Their Discovery and Interpretation. By Holland Hudson, Director, Rosetta van Gelder, Rehabilitation Assistant, Rehabilitation Service. Paper. Pp. 55. New York: National Tuberculosis Association, 1940.

The National Tuberculosis Association recognizes the importance of occupational therapy, has studied the available tests of aptitude and presents them in a reasonably priced manual with full instructions as to how the various tests may be performed. A booklet of this kind has value for counselors in rehabilitation.

War Wounds and Injuries. Edited by E. Fletcher, M.A., M.B., M.R.C.P., Physician, Queen Mary's Hospital for the East End, London, and R. W. Raven, F.R.C.S., Surgeon to Out-Patients, French Hospital, London. With a foreword by Lord Horder. Based on articles in the "Post-Graduate Medical Journal" (Fellowship of Medicine). Cloth. Price, $5. Pp. 262, with 57 illustrations. Baltimore: William Wood & Company, 1940.

This small volume contains articles dealing with practically all aspects of war wounds and injuries except burns and sepsis. Without entering into extensive theoretical discussions or attempting a presentation of controversial points of view the information offered represents the essence of experience gathered during the war of 1914-1918 as well as that more recently acquired in the present war. The contribution is preeminently practical and will undoubtedly prove of value to the younger surgeon called to military duty.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

YELLOW FEVER

To the Editor:—**Please give me information about yellow fever, which I cannot obtain from the sources otherwise available to me. 1. In the absence of complete postmortem examination, is the diagnosis possible through examination of a "core" of the liver tissue obtained with a trocar? 2. How is diagnosis established in convalescent persons? 3. How is a vaccine obtained without identification of the causative organism? 4. How is the rhesus monkey utilized in the study of yellow fever?**

Hermann B. Gessner, M.D., New Orleans.

ANSWER.—1. Yes, with small chance of error, if an adequate specimen, like that obtainable with the "viscerotome," is preserved in solution of formaldehyde U. S. P. diluted 1:10 and examined by a pathologist familiar with yellow fever.

2. For certain diagnosis in cases with recovery, 10 cc. of blood serum should be obtained in the first three or four days of illness and again three weeks after onset or later. The first specimen may be highly infectious and should not touch the skin of the operator. Each specimen should be tested in the laboratory in mice for protective yellow fever antibodies. If the first specimen gives a negative and the second a positive result, the illness is yellow fever. If only the convalescent serum is available a positive result shows merely that the person has had yellow fever at some time, but a negative one rules out yellow fever.

3. The causative agent is a filtrable virus which has been known and studied since 1927. The vaccine most widely used consists of a strain (17 D) of the living virus modified through long cultivation in chick embryo tissues.

4. The rhesus monkey is used in recovering yellow fever virus from man by injections of blood, in studying the effects of the virus in an animal reacting about as man does and in testing the vaccine for safety and effectiveness.

UNDULANT FEVER OR OTHER GASTRO-INTESTINAL DISEASE

To the Editor:—**A woman aged 63 complained of headache, general aching, nausea and epigastric distress, together with a teasing cough and slight coryza. The temperature was 100.4 F. Since a mild epidemic of influenza was prevailing at the time a diagnosis of influenza was made, and under appropriate therapy the temperature dropped to normal and the respiratory symptoms cleared. However, the headache, epigastric distress and backache have persisted unchanged up to the present (six weeks) and a further history disclosed that she has had similar complaints over the past six months. There is an indefinite mass palpable in the epigastric region to the left of the midline, with moderate tenderness. There is a less marked tenderness at the right costal margin over the gallbladder region. The skin is dry and sallow, with a slight icteric tint to the scleras. The rest of the physical examination is negative. There is a definite retention in the stomach, and she is unable to take more than a few mouthfuls of food at a time. Gastrointestinal roentgenograms were reported negative except for the retention. No evidence of malignancy was found. The gastric contents showed normal chemistry. Duodenal drainage has been carried out a number of times, magnesium sulfate, diluted hydrochloric acid and tincture of Carduus mariana being used as stimulants. No B bile has been obtained on any occasion. Flushings of the biliary system with various cholagogues gave no relief. Numerous preparations used to relieve the nausea had no apparent effect. The red count was 5,230,000, white count 8,200, hemoglobin 80 per cent. There is a slight dehydration present. A Hinton test was reported negative. A specimen of blood was reported negative for typhoid and paratyphoid and positive for undulant fever in a titer of 1:80. At the present time I am giving her injections of undulant fever vaccine at four day intervals. As she gets a fairly severe reaction locally, I have not increased the initial dose of 0.2 cc. In view of the failure to obtain B bile, I am continuing to carry out a duodenal drainage once a week. In addition she is getting sulfanilamide 5 grains every four hours. She has no fever at the present time and no night sweats. Her headache is unchanged and quite severe; she still has severe backaches, and the epigastric distress remains, with the anorexia. None of the usual analgesics relieve the headache. Any suggestions as to further laboratory work or therapeutic measures would be greatly appreciated. Economic conditions are such that I would not want to advocate expensive procedures unless they were clearly indicated.**

M.D., New Hampshire.

ANSWER.—The information given is not sufficient to exclude numerous diseases; consequently, many additional laboratory procedures and continued observation may be necessary to arrive at a clinical diagnosis. The symptoms and observations described are compatible with brucellosis (undulant fever) but this diagnosis cannot be considered as definitely established. Undulant fever, as the term implies, is characterized by fever of various types, degrees and duration with a tendency to relapse. This is one of the most constant clinical characteristics of the disease. The patient was apparently known to have had only one febrile episode and this of short duration. This would be a somewhat unusual course in undulant fever. It has been noted that patients with brucellosis are frequently unaware of a considerable degree of fever, and unless the temperature is taken daily at regular intervals both the patient and the family may not suspect that it is elevated. A temperature chart may be of great diagnostic value and if, under these circumstances, the patient's temperature has been and continues to be normal, the significance of the 1:80 agglutination titer is questionable. Such a titer may result from a past infection which is inactive at present. In the event of an active untreated infection the titer is ordinarily found to increase when the agglutination test is repeated at intervals of several weeks. Vaccine and sulfanilamide therapy may affect both the fever and the agglutination titer, and this should be taken into consideration in the interpretation of the findings. The white and differential blood counts may be helpful. The typical blood picture in undulant fever in the absence of secondary infection is that of a leukopenia with a relative lymphocytosis. The spleen is often enlarged but not always palpable. The intradermal test for undulant fever has definite limitations in the diagnosis of an active infection. The skin of practically all persons who have had brucellosis remains permanently allergic to the antigen used in the standard intradermal test. When this allergic response is absent, that is, when the test is negative, it is usually considered strong but not conclusive evidence that the patient has never had a Brucella infection. In the presence of an active brucellosis, the intradermal test is almost always positive and the opsonocytophagic test is negative, whereas when both the intradermal test and the opsonocytophagic test are positive the infection is considered inactive and may, in fact, have completely subsided years before. Investigators, however, do not all agree as to the reliability and interpretation of the opsonocytophagic index, which incidentally is the quantitative determination of the patient's neutrophilic leukocytes to phagocytize Brucella organisms. Furthermore this is not a simple determination, and some experience with the method is usually required. The diagnosis of an active Brucella infection may, indeed, be difficult and can usually be made with absolute certainty only when cultures from the blood, stool or urine yield Brucella organisms. In rare instances the organism has been found in the bile. Unfortunately negative cultures have little significance, since Brucella organisms are not always found in persons proved by their subsequent course to have had an active brucellosis at the time repeated cultures were made. Further details of these tests can be found in Huddelson, I. F.: Brucellosis in Man and Animals, New York, Oxford University Press, 1939.

In view of the fact that the patient may have had influenza six weeks ago and has since then been afebrile, certain noninfectious diseases may merit further consideration. No mention is made of a cholecystogram. Unless the jaundice is severe or the patient is unable to swallow the dye, this might be of value. The history and findings as given could be those of a malignant growth, particularly of the digestive tract, and more specifically of a cancer of the pancreas or the stomach. Carcinoma of the pancreas is frequently difficult to diagnose clinically even when the best laboratory facilities are available. It is sometimes suspected in patients with some degree of icterus which persists and becomes progressively worse, particularly when associated with a severe backache and a suggestive epigastric mass in the absence of a demonstrable intrinsic lesion of the stomach or the duodenum. This impression is not infrequently confirmed at operation or necropsy. The frequent association of cholelithiasis and carcinoma of the pancreas may confuse the clinical picture.

It has often been emphasized that gastric carcinoma may be asymptomatic until a late stage, even when numerous metastases have already occurred. It has also been observed that a small, hardly detectable carcinoma of the stomach may give rise to widespread metastases and that, in fact, the first complaints of a patient may be due to distant metastases. An early or small gastric carcinoma may barely arouse the suspicion of even the most expert roentgenologist, and not uncommonly it is necessary to repeat the roentgenologic examinations one or more times to arrive at a definite opinion.

Since carcinoma of the stomach is one of the most common cancers, it is always well to keep this possibility in mind, particularly in persons over 40 years of age who complain of digestive disturbances of only a few months' duration. The

initial symptoms are often vague and may not direct attention to the stomach primarily. Stools collected while the patient is on a meat-free diet and in the absence of bleeding from the upper respiratory tract usually, but not always, give a positive test for occult blood. When hemorrhoids are present, as is frequently the case in elderly people, it is preferable to test material from the center of a fresh stool. The persistent presence of occult blood in the stool is not diagnostic of any particular condition but demands an explanation. In elderly people it is always suggestive of a gastrointestinal cancer and, unless the bleeding can be satisfactorily explained, a thorough proctoscopic examination is indicated. It should be noted that the passage of a stomach or duodenal tube may in itself result in occult blood in the stool for some days. The presence of free acid in the gastric contents does not exclude the possibility of gastric carcinoma. In some series free acid has been found in almost 50 per cent of the cases of carcinoma of the stomach at the time of diagnosis.

In the event of a malignant obstruction of the biliary tract, jaundice usually becomes progressively more pronounced. In obstruction due to cholelithiasis, jaundice is more apt to fluctuate or subside. This is sometimes best followed by serum bilirubin determinations at intervals of a week or so, and when this method is not available the icterus index can be used.

When free acid is present in the stomach contents of a patient with gastric retention, and chlorides and fluid are lost by vomiting or aspiration, alkalosis may result. The carbon dioxide capacity of the blood is then increased and the serum chloride is decreased. Headache is a common symptom in alkalosis and usually does not improve unless specific therapy is instituted. When parenteral fluids and saline solution are given, the symptoms of alkalosis almost invariably subside and not infrequently the improvement is spectacular.

Cardiorenal vascular disease accompanied by nitrogen retention may also cause severe persistent headaches refractory to almost any form of therapy. However, the patient's blood pressure seems to exclude this possibility, and furthermore the urinalysis would probably have given some indication of this. The patient's blood urea nitrogen level is apt to be elevated in view of the dehydration, and under these circumstances it is often difficult if not impossible to estimate the renal function unless sufficient fluid is given to do a urea clearance test. The fluids would, of course, have to be given parenterally to this patient.

Unfortunately the procedures which may be necessary to arrive at a diagnosis are not all simple. Therapeutic measures must of necessity be supportive until the primary pathologic condition can be recognized. The question arises as to whether the nausea might not be aggravated by sulfanilamide. In view of the dehydration and inability to take sufficient fluids by mouth, parenteral fluids are strongly indicated.

DIAGNOSIS AND TREATMENT OF MÉNIÈRE'S SYNDROME

To the Editor:—**A patient has what is considered Ménière's syndrome. Spinal manometry and ophthalmoscopy reveal nothing of significance. The attacks of vertigo, nausea and vomiting are disabling, especially since the subject tends to be somewhat neurotic. 1. Does impairment of hearing have to be present in order to consider it a true Ménière's syndrome? There is no impairment of hearing. 2. The recent onset precludes consideration of operative intervention at this time. Has any confirmation been obtained regarding the use of electrolytes, orally, for the control of the dizzy spells? Is the method worth trying? If so, what salts are used? Dosage and other pertinent material is requested. 3. Have statistics been published on spontaneous recovery in this affliction or on recovery after various methods of treatment?** **Isidore I. Weiss, M.D., Stockton, Calif.**

ANSWER.—1. Ménière's syndrome is defined as attacks of vertigo of otitic origin associated with tinnitus and deafness. However, it is possible for the tinnitus and deafness to be absent, at least in the early stages.

2. The medical treatment of Ménière's syndrome is based on (*a*) removal of etiologic factors such as chronic middle ear suppuration, foci of infection or allergic factors; (*b*) symptomatic treatment based on the assumption that the periodic attacks of vertigo are due to an edema or increase in intralabyrinthine fluid pressure: restriction of the intake of sodium, especially in the form of sodium chloride, restriction of the fluid intake to 1,000 cc. a day and the administration of potassium chloride or ammonium chloride to stimulate the excretion of sodium in the urine and thus to reduce a tendency for fluid retention in the tissues, since the sodium ion seems to be an important factor in fluid retention. (Dosage: ammonium chloride 3 Gm. with each meal in capsules, 6 capsules, each containing 7½ grains [0.5 Gm.], taken during the meal, three days on, two days off. Or potassium chloride, 2 teaspoons, 25 per cent solution, three times a day. All of these medical measures are worth trying. Not all of them give results in every case.

3. It is a frequently recorded fact that Ménière's disease tends to be self limited and after a variable length of time, months or years, the attacks may cease spontaneously. In some cases the hearing impairment becomes stationary and permanent; in others the hearing improves as the attacks cease. Because of this tendency to spontaneous recovery, operative intervention should be reserved for only the most stubborn and disabling cases of vertigo, and the results of treatment must be interpreted cautiously.

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A summary of the annual literature on Ménière's disease appears in the *Archives of Otolaryngology* each year. The recent work is covered in the issues for December 1939 and for March 1941.

COTTONSEED SENSITIVITY

To the Editor:—**Would you please inform me whether a person found sensitive to cottonseed is to avoid contact with all cotton and finished products, such as bedsheets, pillow cases, dresses and underwear or do the different processes through which cotton passes from the crude to the finished forms destroy the allergic property of the cottonseed embryo?** **Jacob Reicher, M.D., Brooklyn.**

ANSWER.—The cottonseed allergen is not present in the pure cotton fiber. The latter is almost totally insoluble in aqueous mediums. If there are any instances of allergy to such cotton products as bed sheets, pillow cases and underwear they are extremely rare and, when suspected, are probably due not to the cotton itself but to dyes and other finishing products. Of course, when the cotton contains some of the seed particles, such as is found in cotton linters, then the material does have the cottonseed allergen. When raw cotton ages, the dust formed contains a new allergen which is ordinarily called the house dust allergen. People become sensitive to this dust, but this material antigenically has no relation to the cottonseed.

OFFENSIVE FLATUS

To the Editor:—**A healthy white man aged 41 complains of gas which is expelled with an offensive odor. This is the only complaint. It has been present for about two years. Constipation is avoided by taking heavy liquid petrolatum daily. All habits are excellent. The patient does not smoke. He says he wants to live a long time and live comfortably physically. I am unable to relieve this condition. Physical examination reveals no abnormalities. The man eats a balanced diet. What is causing this condition? What diet do you suggest? What medication do you advise? This information is crude, but there is no other information to give.** **M.D., South Carolina.**

ANSWER.—The passage of unusual amounts of foul smelling flatus suggests a dysfunction of the digestive tract which permits unusual amounts of poorly digested or assimilated foods to reach the colon. Intelligent treatment requires a more complete diagnosis. The examination of fecal specimens is required, and this is a procedure most frequently neglected. A highly acid stool containing undigested carbohydrates would indicate a fermentative process and the need for a diet low in carbohydrates. Putrefaction must also be excluded. In any event the use of liquid petrolatum should be stopped, organic causes of the constipation excluded and a normal intestinal function restored with a diet rich in cooked fruits and vegetables. In some persons the habitual use of liquid petrolatum alone may cause considerable disturbance of intestinal digestion and absorption, especially of vitamins, and give rise to a condition such as that described.

OINTMENT BASE FOR SULFATHIAZOLE

To the Editor:—**In the Journal, Jan. 25, 1941, page 536, a formula is given for sulfanilamide ointment. Could sulfathiazole be used instead of sulfanilamide in this formula? If not, is there a formula in which sulfathiazole can be used?** **Ellsworth Wilson, M.D., Highland, Ill.**

ANSWER.—Sulfathiazole cannot be incorporated easily in the ointment base mentioned. Cod liver oil or hydrous wool fat base seem to be more satisfactory for incorporating sulfathiazole.